Official Title: A Phase 2, Double-Blind, Randomized, Placebo-Controlled, Dose-Ranging, Efficacy, and Safety Study of Povorcitinib in Participants With Chronic Spontaneous Urticaria

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Statistical Analysis Plan

INCB 54707-207

A Phase 2, Double-Blind, Randomized, Placebo-Controlled, Dose-Ranging, Efficacy, and Safety Study of Povorcitinib in Participants With Chronic Spontaneous Urticaria

IND Number:	[redacted]
EU CT Number:	**2022-503062-72-00**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803** **United States**
Protocol Version:	**Protocol Version 1 dated 07 MAR 2023**
CRF Approval Date:	**08 OCT 2024**
SAP Version:	**Original**
SAP Author:	[redacted] [redacted] **Biostatistician**
Date of Plan:	**20 MAR 2025**

This study is being conducted in compliance with Good Clinical Practice, including the archiving of essential documents.

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[redacted]

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LIST OF ABBREVIATIONS

Abbreviations and Special Terms	Definition
AAS	angioedema activity score
[redacted]	[redacted]
AE	adverse event
AE-QoL	Angioedema Quality of Life Questionnaire
AESI	adverse event of special interest
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
CI	confidence interval
CPK	creatine phosphokinase
CRF	Case Report Form
CSR	Clinical Study Report
CSU	chronic spontaneous urticaria
CTCAE	Common Terminology Criteria for Adverse Events
[redacted]	[redacted]
DILI	drug-induced liver injury
DLQI	Dermatology Life Quality Index
DMC	Data Monitoring Committee
ECG	electrocardiogram
ECI	event of clinical interest
eCRF	electronic case report form
eDiary	electronic diary
E_{max}	maximum treatment effect over placebo
EOS	end of study
EOT	end of treatment
EOT2	end of treatment during the extension period
[redacted]	[redacted]
EXT	extension
FAS	full analysis set
FDA	Food and Drug Administration
HDL	high-density lipoprotein
HLT	high-level term
HSS	hive severity score
[redacted]	[redacted]
IgE	immunoglobulin E
ISS	itch severity score

Abbreviations and Special Terms	Definition
[redacted]	[redacted]
LDL	low-density lipoprotein
MACE	major adverse cardiovascular event
MCP	multiple-comparison procedure
MCP-mod	multiple-comparison procedure and modeling
MedDRA	Medical Dictionary for Regulatory Activities
MID	minimally important difference
MMRM	mixed model for repeated measures
PC	placebo-controlled
[redacted]	[redacted]
[redacted]	[redacted]
PK	pharmacokinetic(s)
PRO	patient-reported outcome
PT	preferred term
Q	Question
QD	once daily
QTcF	QT interval corrected using Fridericia's formula
SAP	Statistical Analysis Plan
SE	standard error
SMQ	standardized MedDRA query
SOC	standard of care
STD	standard deviation
TEAE	treatment-emergent adverse event
UAS	urticaria activity score
UAS7	urticaria activity score over 7 days
UCT	urticaria control test
ULN	upper limit of normal
VAS	visual analog scale
WHO	World Health Organization
[redacted]	[redacted]

1. INTRODUCTION

This is a Phase 2, multicenter, parallel-group, double-blind, randomized, placebo-controlled, dose-ranging study to evaluate the efficacy and safety of povorcitinib in participants with CSU on stable SOC with second-generation H1 antihistamines over a 12-week PC period followed by a 24-week single-blind EXT period. At baseline, participants will be randomly assigned to receive placebo or povorcitinib 15, 45, or 75 mg QD in a 1:1:1:1 ratio for the PC period. At the start of the EXT period, participants initially randomized to povorcitinib 15, 45, or 75 mg QD will continue povorcitinib at that same dose, and participants initially randomized to placebo will be randomly assigned to povorcitinib 15, 45, or 75 mg QD. Participants will return for a follow-up visit approximately 60 days after their last dose of study drug.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the INCB 54707-207 Protocol.

[redacted]

The details of the analysis methodology of biomarkers and pharmacodynamics and results will appear in a separate report.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 54707-207 Protocol dated 07 MAR 2023 and CRFs approved 08 OCT 2024. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and eCRF versions.

2.2. Study Objectives and Endpoints

Table 1 presents the objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints
Primary	
To evaluate the efficacy of povorcitinib in participants with CSU.	• Change from baseline in the UAS7, defined as the 7-day sum of the individual, daily recorded scores for HSS and ISS, at Week 12.
Secondary	
To further evaluate the efficacy of povorcitinib in participants with CSU.	• Proportion of participants who achieve UAS7 $\leq$ 6 (controlled disease) at Week 12. • Time to first achievement of UAS7 $\leq$ 6 (controlled disease) during the PC period. • Proportion of participants with UAS7 = 0 at Week 12.
Safety	
To evaluate the safety and tolerability of povorcitinib.	• AEs, assessed by changes in vital signs and ECGs and through clinical laboratory sample evaluations and the results of physical examinations.
Exploratory	
[redacted]	

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
Exploratory (continued)	
[redacted]	

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
Exploratory (continued)	
[redacted]	

3. STUDY DESIGN

This is a Phase 2, double-blind, placebo-controlled, multicenter study of povorcitinib in participants with CSU on stable SOC with second-generation H1 antihistamines. The study will enroll approximately 136 participants in a 1:1:1:1 randomization ratio, stratified at baseline by previous anti-IgE biologic use (yes or no), into 1 of 4 treatment groups during the PC period (12 weeks).

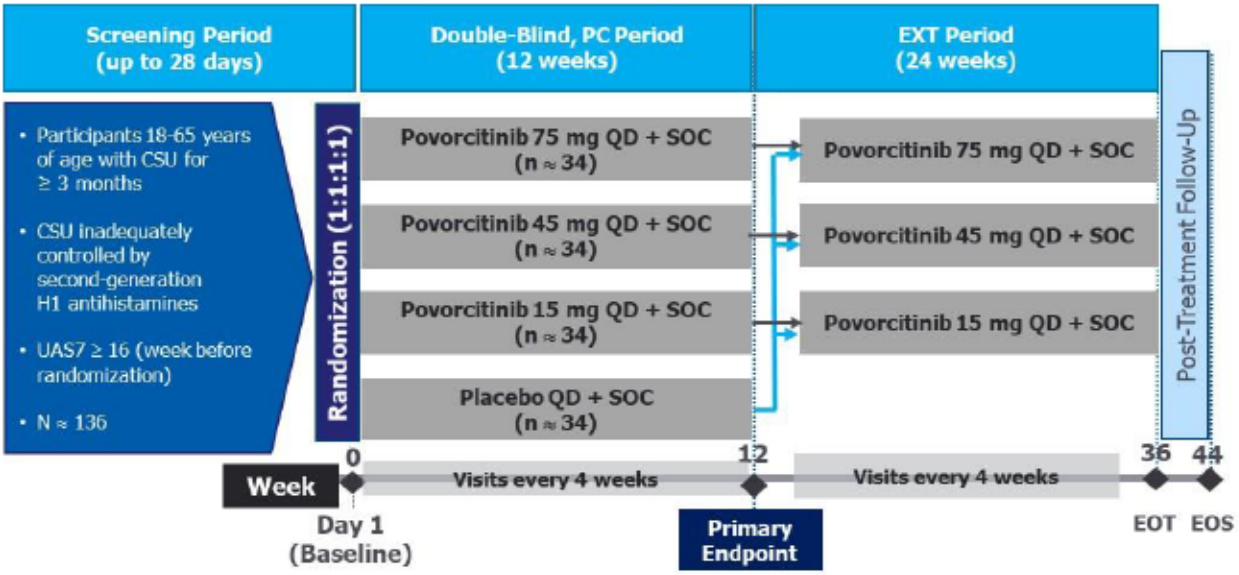
Treatment with study drug will start on Day 1 (baseline). After completing the 12-week PC period, participants will enter the 24-week EXT period. During the EXT period, the participants initially randomized to povorcitinib 15, 45, or 75 mg QD will continue taking povorcitinib at the same dose regimen. The participants initially randomized to placebo will be randomly assigned to take 1 of these 3 dose regimens (ie, povorcitinib 15, 45, or 75 mg QD). Participants, investigators, and the sponsor will remain blinded to each participant's treatment assignment during the PC period. Participants and investigators will continue to remain blinded during the EXT period and post-treatment follow-up period.

Participants will receive study drug until completion of the 36-week treatment period or until one of the criteria for study treatment discontinuation is met. Participants will return for a follow-up visit approximately 60 days after their last dose of study drug.

All participants are required to maintain a stable dose of second-generation H1 antihistamine (SOC) during the study from the time of informed consent until the completion of the post-treatment follow-up visit. The SOC will be determined by the investigator. Further doses of second-generation H1 antihistamines may be used as rescue medication to treat worsening CSU symptoms at any time during the study. A 1-time, short course (maximum duration of 7 days) of glucocorticosteroids may be used as rescue medication after Week 4 in the case of severe exacerbation.

Figure 1 depicts the study design schema.

Figure 1: Study Design Schema



The primary analysis will occur after the primary database lock, when all participants have either completed the Week 12 visit or withdrawn from the study. The sponsor will be unblinded at the time of primary analysis.

The final analysis will occur after the last participant has completed the last visit in the study.

3.1. Randomization

The study will enroll approximately 136 participants in a 1:1:1:1 randomization ratio, stratified at baseline by previous anti-IgE biologic use (yes or no), into 1 of 4 treatment groups during the PC period.

3.2. Control of Type I Error

No multiplicity adjustment will be applied for the statistical tests. Two-sided 95% CIs will be reported for all analyses when appropriate.

3.3. Sample Size Considerations

The sample size is based on the primary efficacy endpoint: change from baseline in the UAS7 at Week 12. Based on a Phase 2b study (Maurer et al 2022), the mean change in UAS7 score at Week 12 is assumed to be −8 in the placebo group and −17 in the povorcitinib 75 mg group, with

a common STD of 13. A sample size of 34 participants per group is sufficient to test for the presence of a dose-response relationship, based on the MCP-mod approach (Bretz et al 2005, Pinheiro et al 2014).

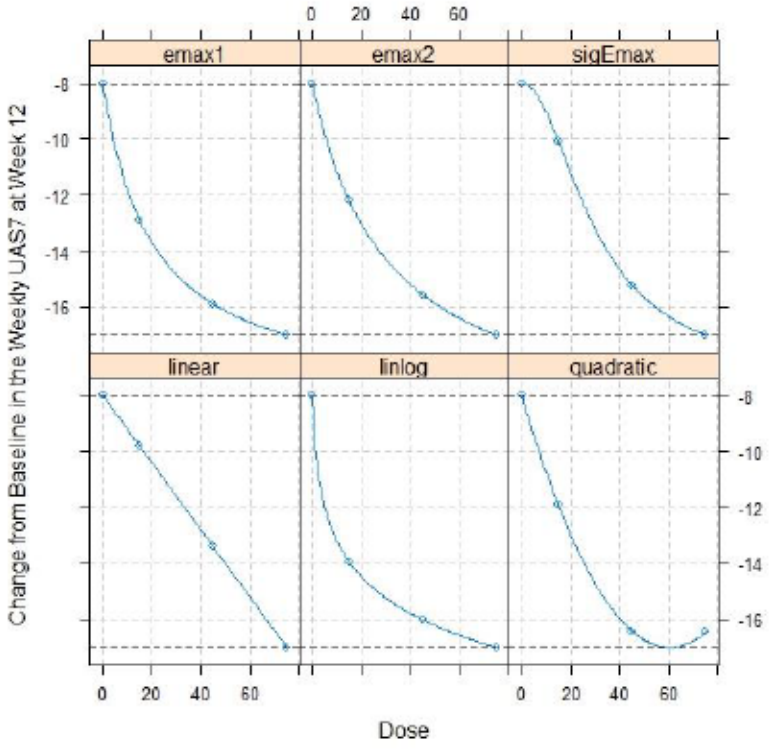
This sample size provides a minimum power of 0.85 to detect a dose effect at a 1-sided 2.5% significance level with the linear, log-linear, E_{max}, and quadratic models prespecified as candidates to characterize the underlying dose-response curve for povorcitinib on the mean change in UAS7 score at Week 12. The set of candidate dose-response models and their corresponding dose-response curves are shown in Table 2 and Figure 2, respectively.

Table 2: Prespecified Candidate Models

Model	$f(d,\theta)$[a]	$f^0(d,\theta)$[b]	Initial Value(s) for Parameter(s)
Linear	$E_0 + \delta d$	d	Not applicable
Linear log-dose	$E_0 + \delta \log(d+1)$	$\log(d+1)$	Not applicable
$E_{max}1$	$E_0 + \frac{E_{max} d}{ED_{50} + d}$	$\frac{d}{ED_{50} + d}$	$ED_{50} = 20$
$E_{max}2$			$ED_{50} = 30$
Sigmoid-E_{max}	$E_0 + \frac{E_{max} d^h}{ED_{50}^h + d^h}$	$\frac{d^h}{ED_{50}^h + d^h}$	$ED_{50} = 30, h = 2$
Quadratic	$E_0 + \beta_1 d + \beta_2 d^2$	$d + \frac{\beta_2}{\lvert\beta_1\rvert} d^2$	$\delta = \frac{\beta_2}{\lvert\beta_1\rvert} = -0.0083$

[a] d is dose (d = 0 for placebo group), θ refers to the vector of model parameters, E_0 is the placebo effect for all candidate models (0.1), E_{max} is the maximum treatment effect over placebo, and ED_{50} is the dose that gives 50% of the maximum effect for the E_{max} model.
[b] Standardized model.

Figure 2: Prespecified Dose-Response Curves



For a reference of different assumptions of STD of the change from baseline in UAS7 at Week 12, the sample sizes and the corresponding minimum power to detect a significant dose-response signal at a 1-sided 2.5% significance level are provided in Table 3.

Table 3: Sample Sizes and Minimum Power Across the 6 Prespecified Candidate Models Under Different Assumptions of Standard Deviation

STD	Sample Size (Placebo:15 mg:45 mg:75 mg)	Minimum Power
11	100 (25:25:25:25)	0.85
12	116 (29:29:29:29)	0.84
13	136 (34:34:34:34)	0.85

3.4. Schedule of Assessments

Refer to Protocol Version 1 dated 07 MAR 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 dose of study drug is administered to participants.

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

For efficacy and safety evaluations during the PC period, baseline is the last nonmissing measurement obtained before or on the day of the first dose.

For participants who cross over into the EXT period, baseline is defined as follows:

- For efficacy evaluation during the EXT period, baseline is the last nonmissing measurement obtained before the first administration of placebo during the PC period.
- For safety evaluation during the EXT period, baseline is the last nonmissing measurement obtained before the first administration of study drug during the EXT period.

For participants who enter the post-treatment follow-up period, baseline for efficacy evaluation is defined as the last nonmissing measurement obtained on or before EOT2.

For participants who are on active drug throughout the study, efficacy and safety baseline is the last nonmissing measurement obtained before or on the day of the first dose.

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

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

4.1.4. Handling of Missing and Incomplete Dates

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 in the eCRF should be used in all relevant listings. The following rules will be used for handling partial dates for analyses requiring dates.

When calculating the time since diagnosis of CSU, a partial CSU diagnosis date will be handled as follows in the calculation:

- If only the day is missing, then the first day of the month will be used.
- If both the month and day are missing, then 01 JAN of the year will be used.
- If the diagnosis date is completely missing, then the time since diagnosis will not be calculated.

When the date of the last dose in a specific period is used in deriving variables, such as duration of treatment or TEAE flag, a missing or partial date of the last dose will be handled as follows:

- If only the day is missing, then the earlier date of the last day of the month or the date that the participant discontinued treatment will be used.
- If both the month and day are missing, then the earlier date of 31 DEC of the year or the date that the participant discontinued treatment will be used.
- Otherwise, the date that the participant discontinued treatment will be used as the date of the last dose.

4.2. Variable Definitions

The following variable will only be calculated if not reported on the eCRF.

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 Medication

Prior medication is defined as any nonstudy medication started before the first dose of study drug.

For the PC period, concomitant medication is defined as any nonstudy medication that is started accordingly:

- Before the date of first administration of povorcitinib or placebo during the PC period and is ongoing or ends on/after the date of first study drug administration during the PC period

  or

- On/after the date of first administration of povorcitinib or placebo during the PC period and before the date of first administration of povorcitinib during the EXT period for participants who enter the EXT period

For the EXT period, concomitant medication is defined as any nonstudy medication that is started accordingly:

- Before the date of first administration of povorcitinib during the EXT period and is ongoing throughout the study or ends on/after the date of first study drug administration during the EXT period

  or

- On/after the date of first administration of povorcitinib during the EXT period

A prior medication could also be classified as both prior and concomitant medication if the end date is on or after the first dose of povorcitinib or placebo during the PC period. In the listing, it will be indicated whether a medication is only prior, only concomitant, 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; 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, STD, median, minimum, and maximum. Descriptive summaries for categorical variables will include the number and percentage of participants in each category.

5.2. Treatment Groups

Table summaries, unless otherwise indicated, will present data by treatment group. The results will be summarized and presented separately for the PC period, EXT period, post-treatment period, and overall period (for safety only) unless otherwise specified.

For the PC period, the treatment groups will be placebo and povorcitinib 15, 45, and 75 mg.

For the EXT period and the post-treatment follow-up period, the treatment groups will be as follows:

- Placebo to povorcitinib 15 mg
- Placebo to povorcitinib 45 mg
- Placebo to povorcitinib 75 mg
- Povorcitinib 15 mg
- Povorcitinib 45 mg
- Povorcitinib 75 mg

For the overall period, the treatment groups will be povorcitinib 15, 45, and 75 mg.

5.3. Analysis Populations

5.3.1. Full Analysis Set Population

The FAS includes all randomized participants who received at least 1 dose of study drug. Treatment groups for this population will be determined according to the treatment they were assigned at the time of randomization.

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

5.3.2. Safety Population

The Safety Population includes all participants who received at least 1 dose of study drug. Treatment groups for this population will be determined according to the actual treatment the participant received regardless of assigned study drug treatment.

All safety analyses for the PC and overall period will be conducted using the Safety Population.

5.3.3. Extension-Evaluable Population

All analyses for the EXT period will be conducted with the EXT-Evaluable Population, which includes all participants who received at least 1 dose of povorcitinib during the EXT period.

5.3.4. Post-Treatment–Evaluable Population

All analyses for the post-treatment period will be conducted with the Post-Treatment–Evaluable Population, which includes all participants who agree to be observed during the post-treatment period.

[redacted]

6. BASELINE, EXPOSURE, AND DISPOSITION

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

6.1. Demographics, Baseline Characteristics, and Disease History

The demographics, baseline characteristics, and disease history will be summarized by treatment groups and overall.

6.1.1. Demographics and Baseline Characteristics

The following demographics will be summarized for the FAS and the EXT-Evaluable Populations: age, age group ($18 \leq$ to ≤ 30, $31 \leq$ to ≤ 40, $41 \leq$ to ≤ 50, $51 \leq$ to ≤ 60, ≥ 61 years), sex, race, ethnicity, weight, height, body mass index, body mass index category (< 25 kg/m^2, ≥ 25 to < 30 kg/m^2, ≥ 30 to < 40 kg/m^2, ≥ 40 to < 50 kg/m^2, and ≥ 50 kg/m^2), and tobacco use (never used, current user, or former user).

6.1.2. Baseline Disease Characteristics and Disease History

The following baseline disease characteristics and disease history will be summarized for all participants in the FAS Population, including, but not limited to the following:

- Disease duration (years)
- CSU family history
- Prior therapy for CSU (yes/no)
- Baseline anti-IgE biologic use (yes/no)
- Baseline IgE
- Baseline high-sensitivity C-reactive protein

- Baseline UAS7
- Baseline UAS7 categories (16-27, moderate; 28- 42, severe)
- Baseline HSS7
- Baseline ISS7
- [redacted]

Note: Disease duration (years) will be calculated as follows:

Disease duration (years) = (date of randomization – date of initial CSU diagnosis + 1) / 365.25.

6.1.3. Medical History

For participants in the FAS Population, medical history will be summarized by treatment group. This summation will include the number and percentage of participants with medical history for each body system/system organ class as documented in the eCRF.

6.1.4. CSU Medical History

For participants in the FAS Population, CSU medical history will be summarized by treatment group.

6.2. Disposition of Participant

The number of participants enrolled by country and/or site will be provided by treatment group and overall.

The following categories will be summarized by treatment group and overall for the FAS Population in the PC period:

- Number (%) of participants who were randomized
- Number (%) of participants who were treated during the PC period
- Number (%) of participants who completed treatment during the PC period
- Number (%) of participants who discontinued treatment with a primary reason for discontinuation of study drug during the PC period
- Number (%) of participants who withdrew from the study with a primary reason for withdrawal from the study during the PC period

The following categories will be summarized by treatment group and overall for the EXT-Evaluable Population during the EXT period:

- Number (%) of participants who were treated during the EXT period
- Number (%) of participants who completed treatment during the EXT period

- Number (%) of participants who discontinued study treatment with a primary reason for discontinuation of study drug during the EXT period
- Number (%) of participants who withdrew from the study with a primary reason for withdrawal from the study during the EXT period

6.3. Protocol Deviations

Protocol deviations recorded will be summarized and listed for the FAS during the PC period and EXT-Evaluable Population during the EXT period.

6.4. Exposure

For participants in the Safety Population during the PC period and the EXT-Evaluable Population during the EXT period, as well as for participants who only received povorcitinib 15, 45, or 75 mg during the overall period, exposure to the study drug will be descriptively summarized by treatment group as follows:

- **Duration of treatment with study drug (days)**: Date of last dose of study drug during the specific period – date of first dose of study drug during the specific period + 1.

The average daily dose of povorcitinib and total actual dose of povorcitinib administered will be summarized by treatment group as follows:

- **Average daily dose of povorcitinib (mg/day):** Total actual povorcitinib dose taken during the specific period (mg) / (duration of treatment with povorcitinib during the specific period [days] – number of interrupted days with povorcitinib during the specific period).
- **Total actual dose of povorcitinib administered (mg):** (Total number of tablets dispensed during the specific period – total number of tablets returned during the specific period) × 15 (mg/tablet) × p_T,

  where p_T denotes the proportion of povorcitinib among the 5 tablets taken daily (ie, $p_T = 0$ [0/5] for the placebo group, 1/5 for the povorcitinib 15 mg group, 3/5 for the povorcitinib 45 mg group, and 5/5 for the povorcitinib 75 mg group).

The total number of tablets dispensed and returned in each period is based on information entered on the Drug Accountability eCRF. Should the dispensed drug not be returned, the actual dose taken, starting from the dispense date of the unreturned drug, will be imputed by the dose taken per the Compliance eCRF.

6.5. Study Drug Compliance

For participants in the Safety and EXT-Evaluable Populations, overall compliance (%) with study drug will be calculated as follows:

Compliance (%) = 100 × (total dose actually taken during the specific period) / (total prescribed dose during the specific period).

The total prescribed dose during the specific period is defined as the sum of the doses prescribed by the investigator accounting for dose interruptions during the specific period; this will be calculated as follows:

(Duration of treatment with study drug during the specific period – number of days with dose interruptions during the specific period) × 5 (tablets/day).

The total actual dose taken in a specific period will be calculated as follows:

Total number of tablets dispensed during the specific period – total number of tablets returned during the specific period.

For more details on the total number of tablets dispensed and returned, see Section 6.4.

6.6. Prior and Concomitant Medication

Prior medications and concomitant medications will be coded using the WHO Drug Dictionary. For the FAS Population during the PC period, both prior and concomitant medications will be summarized by treatment group and overall. For the EXT-Evaluable Population during the EXT period, only concomitant medications will be summarized by treatment group and overall. For participants who received only povorcitinib 15, 45, or 75 mg during the overall period, concomitant medications will be summarized by treatment group and overall. The number and percentage of participants in all populations will be summarized by WHO drug class and WHO drug PT.

7. EFFICACY

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

7.1. General Considerations

All by-visit analyses for the EXT-Evaluable Population will include the follow-up period if the data are available or unless otherwise specified. Likewise, unless otherwise stated, the strata identified in the randomization process will be used in all efficacy analyses.

7.2. Efficacy Parameters

7.2.1. Patient-Reported Outcomes

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

- UAS (see Section 7.2.1.1)
- AAS (see Section 7.2.1.2)
- UCT (see Section 7.2.1.3)
- [redacted]

- [redacted]

7.2.1.1. Urticaria Activity Score

The UAS is a composite, eDiary-recorded score with numeric severity intensity ratings (0 = none to 3 = intense/severe) for 1) the number of hives (ie, HSS) and 2) the intensity of the pruritus (ie, ISS) over the past 24 hours.

The ISS7 is defined as the 7-day sum of the daily ISS scores, and the HSS7 is also defined as the 7-day sum of the daily HSS scores.

The UAS7 is the 7-day sum of the daily UAS. The UAS7 (range: 0-42) is equal to the ISS7 (range: 0-21) plus the HSS7 (range: 0-21; see the scoring guide for further details).

The baseline UAS7 scores will be determined by summing the 7 daily UAS scores before Day 1 (ie, Day −7 to Day −1), divided by the number of nonmissing days, multiplied by 7.

Should more than 2 of the 7 days of the daily UAS scores be missing prior to Day 1, then the baseline UAS7 will be set to missing.

Similarly, the by-visit UAS7 score for postbaseline visits will be determined by summing the 7 daily UAS scores before the visit day. If more than 2 daily UAS scores out of the 7 days before the visit day are missing, the UAS7 at the visit will be set to missing.

For time-to-event endpoints, the UAS7 part will be derived similarly as above, using each nonmissing day as an anchor for any study day after Day 7. Subsequent variables, including achievement of UAS7 ≤ 6, UAS7 ≥ 9.5-point improvement from baseline, HSS7 MID ($\geq$ 5-point) improvement from baseline, and ISS7 MID ($\geq$ 5-point) improvement from baseline, will be calculated for each nonmissing day.

The first day achieving any of the above endpoints is defined as the earliest date of achieving the event. Then, the time to event will be calculated as (date of event – Day 1 date + 1).

Participants who did not achieve the event during the PC period/EXT period will be censored as follows:

- Participants who completed the PC period through Week 12 or the EXT period through Week 36 without having the event will be censored and the censored time will be calculated as (date of last available UAS7 measurement – Day 1 date + 1).

[redacted]

7.2.1.2. Angioedema Activity Score

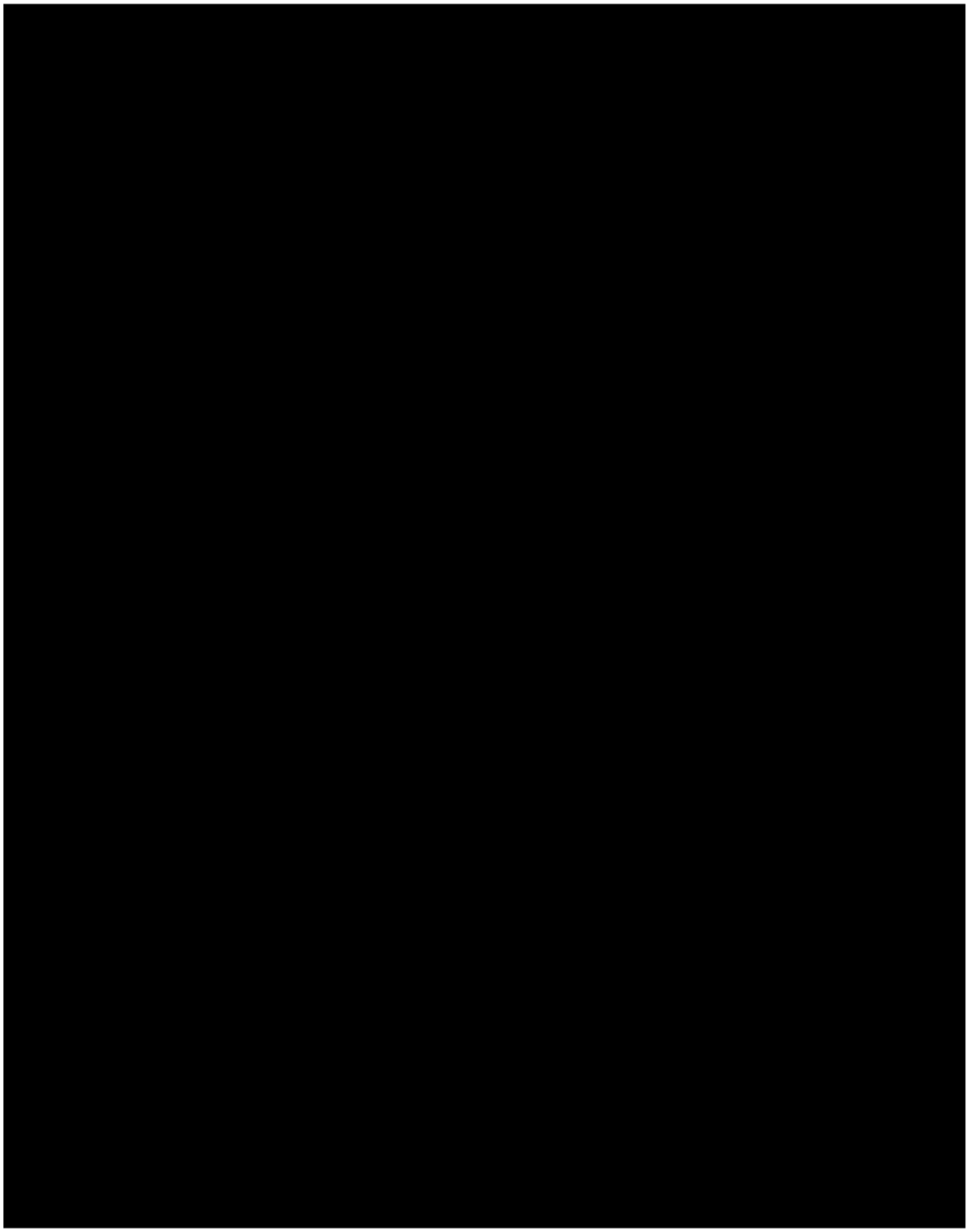
The AAS eDiary records if participants have experienced a swelling episode during the previous 24 hours. If the participant responds yes, further questions are asked covering time of event, physical discomfort, impact on daily activities, appearance, and overall severity.

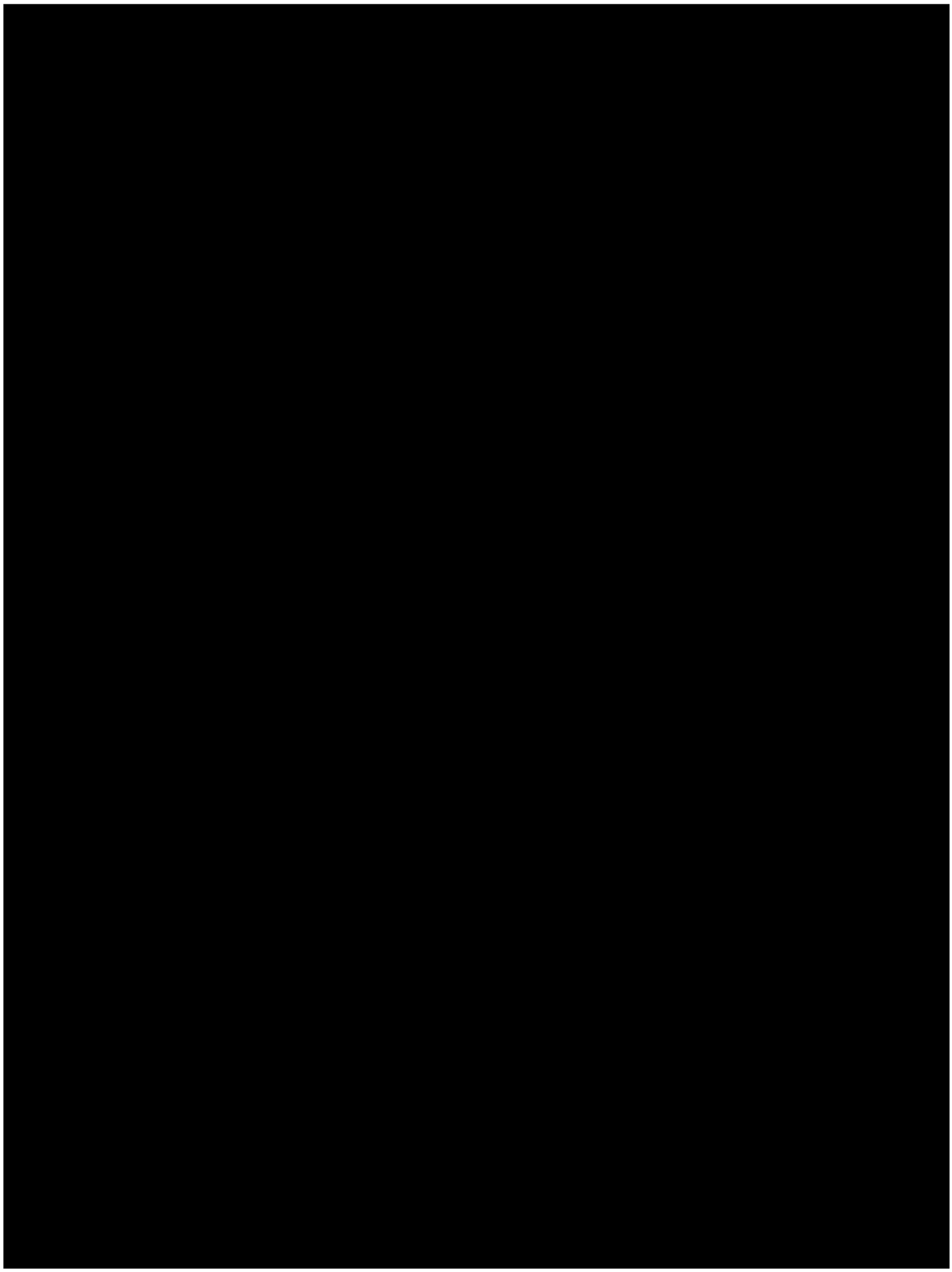
[redacted]

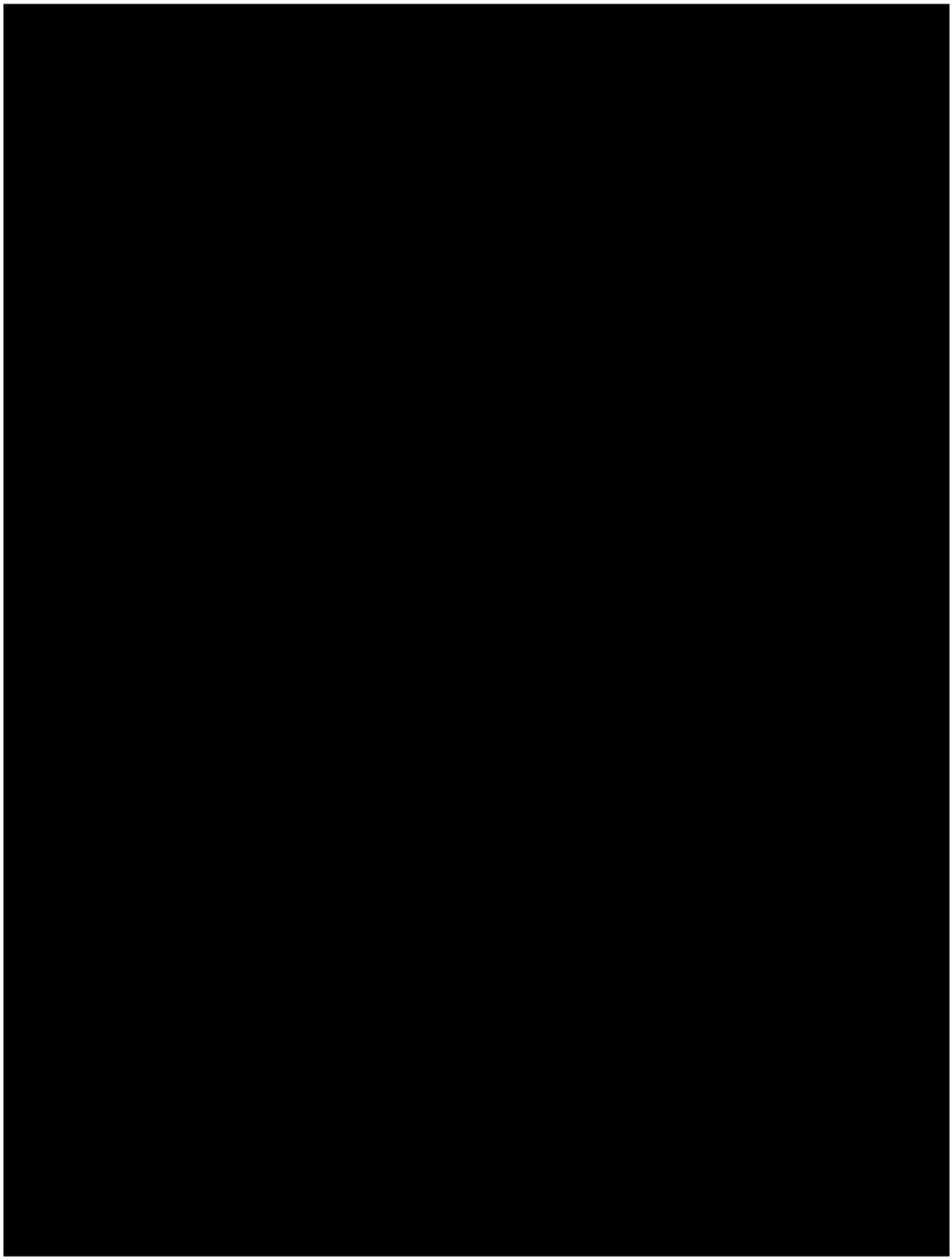
7.2.1.3. Urticaria Control Test

[redacted]

[redacted]







[redacted]

7.3. Analysis of the Primary Efficacy Parameter

The primary efficacy endpoint is the change from baseline in the UAS7, defined as the 7-day sum of the individual, daily recorded scores for HSS and ISS, at Week 12. The primary estimand and corresponding intercurrent strategies are provided in Table 4 and Table 5.

Table 4: Estimand for Primary Endpoint

Primary Endpoint	Population	Treatment	Population-Level Summary
Change from baseline in the weekly UAS7 at Week 12	Participants aged 18 to 65 years who have had a diagnosis of CSU for ≥ 3 months that is inadequately controlled by second-generation H1 antihistamines	Each of the povorcitinib dose groups compared with placebo	The estimated mean change from baseline in UAS7 for each treatment group, as well as the difference in the estimated mean change from baseline in UAS7 score in each active treatment group as compared with the placebo group, at Week 12

Table 5: Intercurrent Events and Strategies for the Primary Estimand

Intercurrent Event	Strategies for Addressing the Intercurrent Event
Treatment discontinuation due to any reason	The data collected for the variable are used regardless of whether the participant discontinues treatment due to any reason (treatment policy strategy)
Initiation of Protocol-allowed rescue medication	The data collected for the variable are used regardless of whether the participant starts the use of any Protocol-allowed rescue medication (treatment policy strategy)

The primary analysis will be performed in the FAS. The mean change from baseline at Week 12 in weekly UAS7 score will be assessed using an MMRM to include all available data at postbaseline visits during the PC period up to Week 12. Participants who have a baseline value and at least 1 postbaseline value during the PC period will be included in the analysis. The MMRM will include change from baseline up to Week 12 as a response variable and the fixed effect of treatment group, randomization stratification factor (previous use of an anti-IgE biologic [yes or no]), visit, treatment-by-visit interaction, and covariates of baseline value and

baseline value by visit interaction. Unstructured covariance matrix will be assumed for the within-participant errors.

Compound symmetry covariance matrix will be used if the model with unstructured variance covariance does not converge. The Kenward-Roger method will be used to estimate the degrees of freedom. Missing data will not be imputed. The least squares mean estimates for each treatment group and the associated covariance matrix obtained from the MMRM will be provided and further used in the generalized MCP-mod framework.

At the MCP stage, contrast test statistics and multiplicity adjusted p-value for the contrast test will be provided for each prespecified candidate model. A dose-response relationship will be declared if at least 1 model among the set of 6 prespecified candidate models is identified to be statistically significant at the level $\alpha = 0.025$ 1-sided trend test. Once a significant dose-response is established, the best model will be selected using Akaike Information Criterion.

At the mod stage, the selected model will be used to obtain the dose-response curve and the 95% CI. The estimated dose-response curve will be presented graphically.

7.3.1. Subgroup Analyses for Primary Endpoint

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

- Sex (male, female)
- Geographic region
- Baseline anti-IgE biologic use

The primary efficacy endpoint will be summarized using descriptive statistics based on the FAS Population for the above subgroups.

7.4. Analysis of the Secondary Efficacy Parameters

The secondary efficacy analysis will be based on the FAS.

7.4.1. Categorical Secondary Efficacy Endpoints

The odds ratios for the proportion of participants with UAS7 ≤ 6 at Week 12 in each of the povorcitinib groups and the placebo group and the corresponding 95% CIs will be assessed using logistic regression with treatment and stratification factor (previous use of an anti-IgE biologic [yes or no]). All participants who have not achieved UAS7 ≤ 6 at Week 12, as well as all participants who are missing postbaseline values, will be defined as nonresponders for the nonresponder imputation analysis.

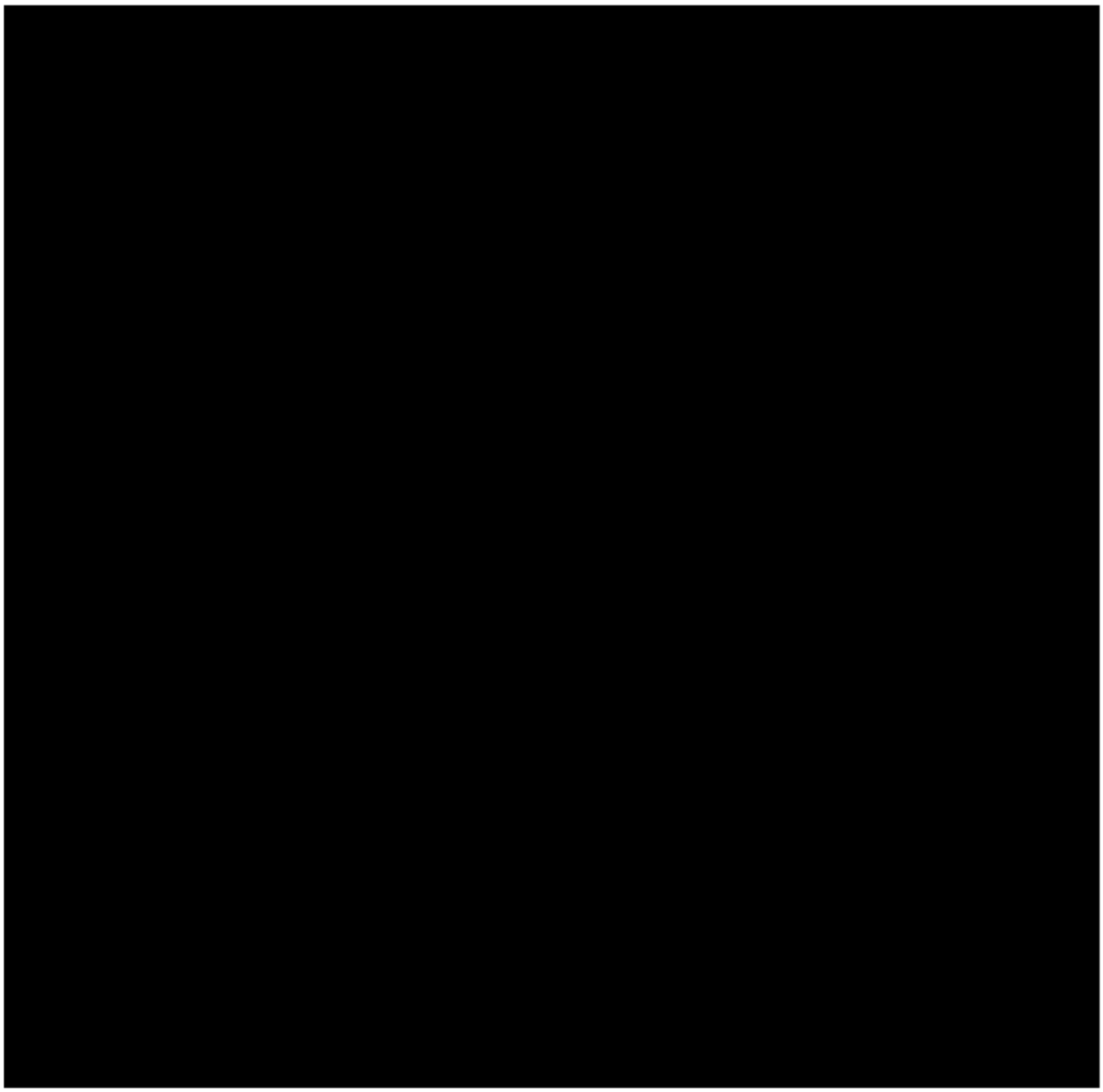
The odds ratios for the proportion of participants with UAS7 = 0 at Week 12 in each of the povorcitinib groups and the placebo group and the corresponding 95% CIs will be assessed using logistic regression with treatment and stratification factor (previous use of an anti-IgE biologic [yes or no]). All participants who have not achieved UAS7 = 0 at Week 12, as well as all participants who are missing postbaseline values, will be defined as nonresponders for the nonresponder imputation analysis.

7.4.2. Time-to-Event Secondary Efficacy Endpoints

Time to first achievement of UAS7 $\leq$ 6 during the PC period is defined as the time from the date of randomization until the earliest date of achieving UAS7 $\leq$ 6 during the PC period. Participants who have not achieved UAS7 $\leq$ 6 during the PC period will be censored at the last available UAS7 measurement time. Summaries of time to first achievement of UAS7 $\leq$ 6 during the PC period will be assessed using the Kaplan-Meier method, and the estimated Kaplan-Meier curve will be displayed graphically.

7.5. Analysis of Exploratory Efficacy Variables

All exploratory efficacy variables will be summarized using descriptive statistics (see Table 1).



9. SAFETY AND TOLERABILITY

Appendix A provides a list of data displays. 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 during the PC period, the EXT-Evaluable Population during the EXT period, and for participants who received only povorcitinib 15, 45, or 75 mg during the overall period unless otherwise specified. 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 the first dose of study drug and up to 30 days after the last dose of study drug. Analysis of AEs will be limited to TEAEs, but data listings will include all AEs regardless of their timing in relation to study drug administration. For purposes of analysis, all AEs will be considered TEAEs unless the AE can unequivocally be defined as not treatment emergent.

A TEAE during the PC period is any AE with a start time after the first dose of study drug during the PC period and until the end of the safety follow-up or prior to the first dose during the EXT period for participants who entered the EXT period.

A TEAE during the EXT period is any AE with a start time after the first dose of study drug during the EXT period and until the end of the EOT2.

For participants who received only povorcitinib 15, 45, or 75 mg during the overall period, a TEAE is any AE with a start time after the first dose of study drug during the PC period and until the EOS.

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the National Cancer Institute CTCAE v5.0. 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 treatment-related TEAEs will also be tabulated.

9.2.2. Adverse Event Summaries

Adverse events will be summarized by treatment group for the Safety Population during the PC period, for the EXT-Evaluable population during the EXT period, and overall for participants who received only povorcitinib 15, 45, or 75 mg during the study.

An overall summary of AEs 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 treatment because of TEAEs
- Number (%) of participants who permanently discontinued study treatment because of TEAEs
- Number (%) of participants who had a fatal TEAE
- Number (%) of participants who had a TEAE requiring concomitant medication

The following summaries will be produced by MedDRA term (if 10 or fewer participants appear in a table, a listing may be appropriate):

- Summary of TEAEs by MedDRA SOC and PT
- Summary of TEAEs by MedDRA PT in decreasing order of frequency
- Summary of TEAEs by MedDRA SOC, PT, and maximum severity
- Summary of TEAEs by MedDRA SOC, PT, and CTCAE grade category
- Summary of Grade 3 or higher TEAEs by MedDRA SOC and PT
- Summary of Grade 3 or higher TEAEs by MedDRA PT in decreasing order of frequency
- Summary of serious TEAEs by MedDRA SOC and PT
- Summary of serious TEAEs by MedDRA PT in decreasing order of frequency
- Summary of treatment-related TEAEs by MedDRA SOC and PT
- Summary of treatment-related TEAEs by MedDRA PT in decreasing order of frequency
- Summary of Grade 3 or higher treatment-related TEAEs by MedDRA SOC and PT
- Summary of treatment-related serious TEAEs by MedDRA SOC and PT
- Summary of TEAEs with a fatal outcome by MedDRA SOC and PT
- Summary of TEAEs leading to dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of study drug by MedDRA SOC and PT

9.2.3. Adverse Events of Special Interest

Incyte defines AESIs and ECIs as a subset of TEAEs that investigators must rapidly communicate to Incyte for further evaluation. The AESI categories and the search strategy of each AESI are provided in Table 6. A separate SMQ file that includes all search strategies will be provided separately. The number and percentage of participants who have any AESI will be summarized.

Table 6: Search Strategies for Adverse Events of Special Interest

Adverse Event of Special Interest Category	Search Strategy
Serious infections	Serious AEs under SOC "Infections and Infestations"
Opportunistic infections	SMQ narrow "Opportunistic Infections"
Herpes zoster	Custom PT search strategy based on the HLT "Herpes viral infections" (refer to SMQ file)
Tuberculosis	HLT "Tuberculosis infections"
Malignancy (all types)	SMQ narrow "Malignant Tumors"
Cardiovascular events (eg, MACE)	MACE custom PT search (refer to SMQ file)
Other embolic and thrombotic events (eg, pulmonary embolism, deep vein thrombosis, thrombosis, cerebrovascular events)	SMQ "Embolic and thrombotic events"

9.2.4. Events of Clinical Interest

An ECI is an AE that Incyte wishes to document in an organized manner for monitoring or understanding. The ECI categories and the search strategy of each ECI are provided in Table 7.

Table 7: Search Strategies for Events of Clinical Interest

Event of Clinical Interest Category	Search Strategy
Increased serum creatinine (> 3 × ULN or > 3 × baseline) and renal disfunction	• Laboratory parameter: Identify all participants with outlier laboratory test values • PT assessment: custom SMQ based on SMQ broad "Acute renal failure" (refer to SMQ file)
Hepatic events and increased hepatic transaminases (> 5 × ULN)	• Laboratory parameter: Identify all participants with outlier laboratory test values • PT assessment: SMQ narrow "Drug-related hepatic disorders" comprehensive search
Increased CPK (> 5 × ULN)	• Laboratory parameter: Identify all participants with outlier laboratory test values • PT assessment: custom SMQ based on SMQ narrow "Rhabdomyolysis/myopathy" (refer to SMQ file)
Acne	Custom PT search (refer to SMQ file)

The ECIs of increased serum creatinine, increased hepatic transaminases, and increased CPK will be predominantly laboratory parameter–based analyses assessing outlier participants. The number and percentage of participants who have increased serum creatinine, ALT, AST, or CPK will be summarized or listed.

In addition, a separate PT search will supplement the laboratory-based analysis. The number and percentage of participants who have any relevant PTs will be summarized or listed.

9.3. Clinical Laboratory Tests

9.3.1. Laboratory Value Definitions

Laboratory values, change from baseline values, and percent change from baseline values will be summarized descriptively by visit, and non-numeric test values will be tabulated when necessary. Baseline will be determined according to Section 4.1.3. 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

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 nonmissing laboratory values for a participant's particular test at a scheduled visit, central laboratory values have higher priority over local laboratory values. If a tie still exists, the laboratory value with the smallest laboratory sequence number will be used in by-visit summaries. In addition, box plots will be provided for creatine kinase, hemoglobin, hematocrit, platelet count, high-sensitivity C-reactive protein, IgE, lymphocyte absolute count, neutrophil absolute count, white blood cell count, basophil cell count, eosinophil cell count, total cholesterol, HDL, LDL, HDL/LDL ratio, ALT, and AST.

For test results that will be summarized with available normal ranges, the number and percentage of participants with laboratory values that are 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. The denominator for the percentage calculation will use the number of participants in the baseline category (ie, low, high, normal, missing) as the denominator for the percentage in each of the categories during the study.

Severity grades will be assigned to laboratory test values based on the numerical component of CTCAE v5. Shift tables will also be presented showing change in CTCAE grade from baseline to the worst grade postbaseline. Separate summaries for abnormally high and abnormally low laboratory values will be provided when the laboratory parameter has both high and low grading criteria. The denominator for the percentage calculation will be the number of participants in the baseline category. The number of participants who experienced worsening of laboratory abnormalities will be summarized by maximum severity.

9.3.3. Potentially Clinically Important Laboratory Values

Criteria for potentially clinically important laboratory values are listed in Table 8. The number and percentage of participants with postbaseline laboratory values that meet each criterion will be summarized at each scheduled visit by treatment group. Participants with potentially clinically important laboratory values will also be listed.

Table 8: Criteria for Potentially Clinically Important Laboratory Values

Laboratory Parameter	Grade (Criteria)
Hemoglobin	Grade 2 (80 to < 100 g/L) Grade 3 (< 80 g/L)
Lymphocytes	Grade 2 (0.5 to < 0.8 × 10^9/L) Grade 3 (0.2 to < 0.5 × 10^9/L) Grade 4 (< 0.2 × 10^9/L)
Neutrophils	Grade 2 (1.0 to < 1.5 × 10^9/L) Grade 3 (0.5 to < 1.0 × 10^9/L) Grade 4 (< 0.5 × 10^9/L)
Platelets	Grade 2 (50 to < 75 × 10^9/L) Grade 3 (25 to < 50 × 10^9/L) Grade 4 (< 25 × 10^9/L)
Creatinine	Grade 2 (> 1.5 to 3 × ULN or > 1.5 to 3 × baseline) Grade 3 (> 3 to 6 × ULN or > 3 × baseline) Grade 4 (> 6 × ULN)
Creatine kinase	Grade 2 (> 2.5 to 5 × ULN) Grade 3 (> 5 to 10 × ULN) Grade 4 (> 10 × ULN)
ALT AST	Grade 3 (> 5 to 10 × ULN) Grade 3 (> 5 to 10 × ULN)
Estimated glomerular filtration rate	Grade 3 (15 to < 30 mL/min/1.73 m^2)

9.3.4. Potential Drug-Induced Liver Injury Events

According to FDA's guidance on drug-induced liver injury (2009), the criteria for potential DILI events include the following:

- ALT ≥ 3 × ULN
- ALT ≥ 5 × ULN
- ALT ≥ 10 × ULN
- ALT ≥ 20 × ULN
- AST ≥ 3 × ULN
- AST ≥ 5 × ULN
- AST ≥ 10 × ULN
- AST ≥ 20 × ULN

- ALT or AST ≥ 3 × ULN
- ALT or AST ≥ 5 × ULN
- ALT or AST ≥ 10 × ULN
- ALT or AST ≥ 20 × ULN
- ALP ≥ 1.5 × ULN
- Total bilirubin ≥ 2 × ULN
- ALT and/or AST ≥ 3 × ULN and total bilirubin ≥ 2 × ULN

Note that the combination of values needs to be measured on the same day.

The number and percentage of participants with postbaseline liver-specific function test values that meet these criteria will be presented at each scheduled visit by treatment group. Participants with potential DILI events will also be listed.

9.3.5. Potential Hy's Law Events

Participants with elevated ALT or AST ≥ 3 × ULN and ALP ≤ 2 × ULN accompanied by total bilirubin > 2 × ULN at the same visit will be listed and plotted by treatment group.

9.4. Vital Signs

At each scheduled visit, change, and percentage change from baseline for vital signs, including systolic blood pressure, diastolic blood pressure, pulse, temperature, respiratory rate, and weight, will be summarized descriptively. Baseline will be determined according to Section 4.1.3.

Normal ranges for vital sign values are defined in Table 9. For participants exhibiting vital sign abnormalities, the abnormal values will be listed along with their assigned treatment group. Alert vital signs are defined as an absolute value outside the defined normal range and percentage change > 25%. Note that the definition of alert vital signs does not apply for body temperature and weight. The abnormal values for participants exhibiting alert vital sign abnormalities will be listed.

Table 9: Normal Ranges for Vital Sign Values

Parameter	High Threshold	Low Threshold
Systolic blood pressure	≤ 155 mm Hg	≥ 85 mm Hg
Diastolic blood pressure	≤ 100 mm Hg	≥ 40 mm Hg
Pulse	≤ 100 bpm	≥ 45 bpm
Temperature	≤ 38°C	≥ 35.5°C
Respiratory rate	≤ 24 breaths/min	≥ 8 breaths/min

9.5. Electrocardiograms

Twelve-lead ECGs, including PR, QT, QRS, and QTcF intervals, will be obtained for each participant during the study. Values at each scheduled visit, change, and percentage change from baseline will be summarized for each ECG parameter. Baseline will be determined as the average of all nonmissing values before the first administration of povorcitinib or placebo.

Normal ranges for ECG values are defined in Table 10. The ECG values will also be considered abnormal if the absolute percentage change from baseline is > 25% (30% for QRS interval). Participants exhibiting ECG abnormalities will be listed with study visit and assigned treatment group. Abnormal values for participants with alert ECG values, defined as both the absolute value and the percentage change from baseline being outside normal ranges, will be identified and listed. Outliers of QT and QTcF values, defined as absolute values > 450 milliseconds, > 500 milliseconds, or change from baseline > 30 milliseconds, will be summarized.

Table 10: Normal Ranges for Electrocardiogram Intervals

Parameter	High Threshold	Low Threshold
PR	≤ 220 ms	≥ 75 ms
QT	≤ 500 ms	≥ 300 ms
QRS	≤ 120 ms	≥ 50 ms
QTcF	≤ 450 ms	≥ 295 ms

10. INTERIM ANALYSES

No formal interim analysis is planned in this study. However, preplanned analyses of safety will be provided to an internal DMC as specified in the DMC charter. The process by which the DMC will review data and make recommendations and decisions will be documented in the DMC charter.

10.1. Overview of Interim Analyses

No formal interim analysis is planned in this study.

11. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 11.

Table 11: Statistical Analysis Plan Versions

SAP Version	Date
Version 1	20 MAR 2025

11.1. Changes to Protocol-Defined Analyses

The endpoint language in the Protocol referring to the following endpoints is not correctly worded for an endpoint.

- AEs, assessed by changes in vital signs and ECGs and through clinical laboratory sample evaluations and the results of physical examinations
- Proportion of participants who achieve UAS7 $\leq$ 6 (controlled disease) at Week 12
- Proportion of participants with ISS7/HSS7/UAS7 = 0 at Week 12
- Proportion of participants who achieve UAS7 $\leq$ 6 at Week 12 and maintain or improve their response at every visit through to Week 36 or EOT2
- Proportion of participants who achieve UAS7 = 0 at Week 12 and maintain their response at every visit through to Week 36 or EOT2
- [redacted]
- Proportion of participants requiring treatment of CSU with corticosteroids from baseline up to Week 36
- Proportion of participants requiring rescue treatment of CSU with additional second-generation H1 antihistamine from baseline up to Week 36
- Proportion of participants using rescue medication during the post-treatment follow-up period (EOT2 to EOS)
- [redacted]
- [redacted]

The endpoint should specify participant-level data to be analyzed, such as

- TEAEs and changes in clinical laboratory evaluations, vital signs, ECGs, and physical examination findings
- UAS7 $\leq$ 6 (controlled disease) at Week 12
- ISS7/HSS7/UAS7 = 0 at Week 12
- UAS7 $\leq$ 6 at Week 12 and maintenance or improvement of response at every visit through to Week 36 or EOT2.
- UAS7 = 0 at Week 12 and maintenance of response at every visit through to Week 36 or EOT2

- [redacted]
- Participants requiring treatment of CSU with corticosteroids from baseline up to Week 36
- Participants requiring rescue treatment of CSU with additional second-generation H1 antihistamine from baseline up to Week 36
- Participants requiring rescue medication usage during the post-treatment follow-up period (EOT2 to EOS)
- [redacted]
- [redacted]

In future protocols, this language will be updated to better reflect the participant-level data for the analyses.

[redacted]

11.2. Changes to the Statistical Analysis Plan

Not applicable.

12. REFERENCES

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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 CSR. Shells are provided in a separate document for tables that are not in the most current Standard Safety Tables. In-text tables are identical in structure and content as appendix tables but follow a Rich Text Format.

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
1.1.1	Analysis Populations	All Screened	X
1.1.1.1	Screening Disposition	All Screened	X
1.1.2.x	Summary of Participant Disposition During the PC Period	FAS/EXT-Evaluable	X
1.1.3	Summary of Number of Participants Enrolled by Country and Site	FAS	X
1.1.4.x	Summary of Protocol Deviations During the PC Period	FAS/EXT-Evaluable	X
1.2.x	Summary of Demographics and Baseline Characteristics During the PC Period	FAS/EXT-Evaluable	X
1.3.1	Summary of Baseline Disease Characteristics	FAS	X
1.4.1	Summary of Prior Medications	FAS	X
1.4.2	Summary of Concomitant Medications During the PC Period	FAS/EXT-Evaluable	X
1.5.1	Summary of General Medical History	FAS	X
1.5.2	Summary of Chronic Spontaneous Urticaria Disease History	FAS	X
Efficacy			
2.1.1.x	Summary and Analysis of UAS7 by Visit	FAS/EXT-Evaluable	
2.1.2	Summary of UAS7 by Visit and Sex	FAS	
2.1.3	Summary of UAS7 by Visit and Geographic Region	FAS	
2.1.4	Summary of UAS7 by Visit and Baseline Anti-IgE Biologic Use	FAS	
2.2.1.1.x	Summary and Analysis of Proportion of Participants Who Achieved UAS7 $\leq$ 6 (Controlled Disease) by Visit	FAS/EXT-Evaluable	
2.2.1.2	Summary of Time to First Achievement of UAS7 $\leq$ 6 (Controlled Disease) During the PC Period	FAS	
2.2.1.3.x	Summary and Analysis of Proportion of Participants With UAS7 = 0 by Visit	FAS/EXT-Evaluable	
2.3.1.1.x	Summary of Change From Baseline in HSS7 by Visit	FAS/EXT-Evaluable	
2.3.1.2.x	Summary of Proportion of Participants With HSS7 = 0 by Visit	FAS/EXT-Evaluable	
2.3.1.3	Summary of Time to First Achievement of HSS7 MID ($\geq$ 5-Point) Improvement From Baseline Up to Week 36	FAS	

Table No.	Title	Population	Standard
2.3.1.4	Summary of Change From Baseline in Weekly HSS7 During the Post-Treatment Follow-Up Period (EOT2 to EOS)	Post-Treatment–Evaluable	
2.3.2.1.x	Summary of Change from Baseline in ISS7 by Visit	FAS/EXT-Evaluable	
2.3.2.2.x	Summary of Proportion of Participants with ISS7 = 0 by Visit	FAS/EXT-Evaluable	
2.3.2.3	Summary of Time to First Achievement of ISS7 MID (≥ 5-Point) Improvement From Baseline Up to Week 36	FAS	
2.3.2.4	Summary of Change From Baseline in Weekly ISS7 During the Post-Treatment Follow-Up Period (EOT2 to EOS)	Post-Treatment–Evaluable	
[redacted]			
2.3.4.1	Summary of Time to First Achievement of UAS7 ≥ 9.5-Point Improvement From Baseline Up to Week 36	FAS	
2.3.4.2	Summary of Proportion of Participants Who Achieved UAS7 ≤ 6 at Week 12 and Maintained or Improved Their Response at Every Visit Through to Week 36 or EOT2	FAS	
2.3.4.3	Summary of Proportion of Participants Who Achieved UAS7 = 0 at Week 12 and Maintained Their Response at Every Visit Through to Week 36 or EOT2	FAS	
[redacted]			

Table No.	Title	Population	Standard
[redacted]			
2.3.13.1	Summary of Proportion of Participants Requiring Treatment of Chronic Spontaneous Urticaria With Corticosteroids From Baseline Up to Week 36	FAS	
2.3.13.2	Summary of Proportion of Participants Requiring Rescue Treatment of Chronic Spontaneous Urticaria With Additional Second-Generation H1 Antihistamines From Baseline Up to Week 36	FAS	
2.3.13.3	Summary of Time to First Use of Rescue Medication From Baseline Up to Week 36	FAS	
2.3.13.4	Summary of Proportion of Participants Using Rescue Medication During the Post-Treatment Follow-Up Period (EOT2 to EOS)	Post-Treatment–Evaluable	
2.3.13.5	Summary of Time to Use of Rescue Medication During the Post-Treatment Follow-Up Period (EOT2 to EOS)	Post-Treatment–Evaluable	
Safety			
3.1.1.x	Summary of Exposure During the PC Period	Safety/EXT-Evaluable	X
3.1.1.3	Summary of Exposure for Participants Who Received Only Povorcitinib Throughout Study Participation (Overall Period)	Safety	X
3.1.2.x	Summary of Study Drug Compliance During the PC Period	Safety/EXT-Evaluable	X
3.2.1.x	Overall Summary of Treatment-Emergent Adverse Events During the PC Period	Safety/EXT-Evaluable	X
3.2.1.3	Overall Summary of Treatment-Emergent Adverse Events for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.2.x	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term During the PC Period	Safety/EXT-Evaluable	X
3.2.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.3.x	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency During the PC Period	Safety/EXT-Evaluable	X

Table No.	Title	Population	Standard
3.2.3.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.4.x	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity During the PC Period	Safety/EXT-Evaluable	X
3.2.4.3	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.5.x	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and CTCAE Grade Category During the PC Period	Safety/EXT-Evaluable	X
3.2.5.3	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and CTCAE Grade Category for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.6.x	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term During the PC Period	Safety/EXT-Evaluable	X
3.2.6.3	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.7.x	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency During the PC Period	Safety/EXT-Evaluable	X
3.2.7.3	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.8.x	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term During the PC Period	Safety/EXT-Evaluable	X
3.2.8.3	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.9.x	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency During the PC Period	Safety/EXT-Evaluable	X
3.2.9.3	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.10.x	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term During the PC Period	Safety/EXT-Evaluable	X

Table No.	Title	Population	Standard
3.2.10.3	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.11.x	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency During the PC Period	Safety/EXT-Evaluable	X
3.2.11.3	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.12.x	Summary of Grade 3 or Higher Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term During the PC Period	Safety/EXT-Evaluable	X
3.2.12.3	Summary of Grade 3 or Higher Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.13.x	Summary of Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term During the PC Period	Safety/EXT-Evaluable	X
3.2.13.3	Summary of Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.14.x	Summary of Treatment-Emergent Adverse Events with a Fatal Outcome by MedDRA System Organ Class and Preferred Term During the PC Period	Safety/EXT-Evaluable	X
3.2.14.3	Summary of Treatment-Emergent Adverse Events with a Fatal Outcome by MedDRA System Organ Class and Preferred Term for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.15.x	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption by MedDRA System Organ Class and Preferred Term During the PC Period	Safety/EXT-Evaluable	X
3.2.15.3	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption by MedDRA System Organ Class and Preferred Term for Participants Who Received Only Povorcitinib During Study Participation	Safety	X
3.2.16.x	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term During the PC Period	Safety/EXT-Evaluable	X
3.2.16.3	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term for Participants Who Received Only Povorcitinib 15,45, or 75 mg During Study Participation	Safety	X
3.2.17.x	Summary of Treatment-Emergent Adverse Events of Special Interest by Category and MedDRA Preferred Term During the PC Period	Safety/EXT-Evaluable	

Table No.	Title	Population	Standard
3.2.17.3	Summary of Treatment-Emergent Adverse Events of Special Interest by Category and MedDRA Preferred Term for Participants Who Received Only Povorcitinib During Study Participation	Safety	
3.2.18.x	Summary of Treatment-Emergent Adverse Events of Special Interest Leading to Dose Interruption by Category and MedDRA Preferred Term During the PC Period	Safety/EXT-Evaluable	
3.2.18.3	Summary of Treatment-Emergent Adverse Events of Special Interest Leading to Dose Interruption by Category and MedDRA Preferred Term During the Overall Study Period for Participants Who Received Only Povorcitinib During Study Participation	Safety	
3.2.19.x	Summary of Treatment-Emergent Adverse Events of Special Interest Leading to Discontinuation of Study Drug by Category and MedDRA Preferred Term During the PC Period	Safety/EXT-Evaluable	
3.2.19.3	Summary of Treatment-Emergent Adverse Events of Special Interest Leading to Discontinuation of Study Drug by Category and MedDRA Preferred Term During the Overall Study Period for Participants Who Received Only Povorcitinib During Study Participation	Safety	
3.2.20.x	Summary of Treatment-Emergent Events of Clinical Interest (PT Component) by Category and MedDRA Preferred Term During the PC Period	Safety/EXT-Evaluable	
3.2.20.3	Summary of Treatment-Emergent Events of Clinical Interest (PT Component) by Category and MedDRA Preferred Term for Participants Who Received Only Povorcitinib During Study Participation	Safety	
3.3.1.1.x	Summary of Laboratory Values - Hematology	Safety/EXT-Evaluable	X
3.3.1.2.x	Summary of Laboratory Values - Chemistry	Safety/EXT-Evaluable	X
3.3.1.3.x	Summary of Laboratory Values - Lipid Panel	Safety/EXT-Evaluable	X
3.3.14	Summary of Laboratory Values - Coagulation	Safety/EXT-Evaluable	X
3.3.1.5	Summary of Laboratory Values - Other	Safety/EXT-Evaluable	X
3.3.2.1.x	Shift Summary of Hematology Laboratory Values - to the Worst Abnormal Value	Safety/EXT-Evaluable	X
3.3.2.2.x	Shift Summary of Chemistry Laboratory Values - to the Worst Abnormal Value	Safety/EXT-Evaluable	X
3.3.2.3.1	Shift Summary of Lipid Panel Laboratory Values - to the Worst Abnormal Value	Safety	X
3.3.3.1.x	Shift Summary of Hematology Laboratory Values in CTCAE Grade - to the Worst Grade Abnormal Value	Safety/EXT-Evaluable	X
3.3.3.2.x	Shift Summary of Chemistry Laboratory Values in CTCAE Grade - to the Worst Grade Abnormal Value	Safety/EXT-Evaluable	X
3.3.3.3.1	Shift Summary of Lipid Panel Laboratory Values in CTCAE Grade - to the Worst Grade Abnormal Value	Safety	X

Table No.	Title	Population	Standard
3.3.4.x	Summary of Potentially Clinically Important Laboratory Values by Visit	Safety/EXT-Evaluable	X
3.3.5.x	Summary of Potential Drug-Induced Liver Injury Events by Visit	Safety/EXT-Evaluable,	
3.4.1.x	Summary of Systolic Blood Pressure During the PC Period	Safety/EXT-Evaluable	X
3.4.2.x	Summary of Diastolic Blood Pressure During the PC Period	Safety/EXT-Evaluable	X
3.4.3.x	Summary of Pulse During the PC Period	Safety/EXT-Evaluable	X
3.4.4.x	Summary of Respiratory Rate During the PC Period	Safety/EXT-Evaluable	X
3.4.5.x	Summary of Body Temperature During the PC Period	Safety/EXT-Evaluable	X
3.5.1.1.x	Summary of PR Interval (ms) From 12-Lead ECG by Visit During the PC Period	Safety/EXT-Evaluable	X
3.5.1.2.x	Summary of QRS Interval (ms) From 12-Lead ECG by Visit During the PC Period	Safety/EXT-Evaluable	X
3.5.1.3.x	Summary of QT Interval (ms) From 12-Lead ECG by Visit During the PC Period	Safety/EXT-Evaluable	X
3.5.1.4.x	Summary of QTcF Interval (ms) From 12-Lead ECG by Visit During the PC Period	Safety/EXT-Evaluable	X
3.5.1.5.x	Summary of Heart Rate (bpm) From 12-Lead ECG by Visit During the PC Period	Safety/EXT-Evaluable	X
3.5.1.6.x	Summary of Clinically Significant ECG Abnormality by Visit During the PC Period	Safety/EXT-Evaluable	X

Figures

Figure No.	Title	Population
4.1.1.1	Least Squares Mean (± SE) Change From Baseline in UAS7 by Visit and Treatment Group During the PC Period	FAS
4.1.1.2.x	Mean (± SE) Change From Baseline in UAS7 by Visit and Treatment Group	FAS/EXT-Evaluable
4.1.2.1	Proportion of Participants Who Achieved UAS7 ≤ 6 (Controlled Disease) by Visit During the PC Period Using Nonresponder Imputation	FAS
4.1.2.2.x	Proportion of Participants Who Achieved UAS7 ≤ 6 (Controlled Disease) by Visit Using Observed Values	FAS/EXT-Evaluable
4.1.3.1	Proportion of Participants Who Achieved UAS7 = 0 (Controlled Disease) by Visit During the PC Period Using Nonresponder Imputation	FAS
4.1.3.2.x	Proportion of Participants Who Achieved UAS7 = 0 (Controlled Disease) by Visit Using Observed Values	FAS/EXT-Evaluable
4.1.4	Kaplan-Meier Curve of the Time to First Achievement of UAS7 ≤ 6 (Controlled Disease) During the PC Period	FAS

Figure No.	Title	Population
4.1.5	Kaplan-Meier Curve of the Time to First Achievement of UAS7 ≥ 9.5 (Controlled Disease) During the PC Period	FAS
4.2.1.1	Proportion of Participants Who Achieved ISS7 = 0 (Controlled Disease) by Visit During the PC Period Using Nonresponder Imputation	FAS
4.2.1.2	Kaplan-Meier Curve of the Time to First Achievement of ISS7 MID (≥ 5-Point) Improvement From Baseline Up to Week 36	FAS
4.2.2.1	Proportion of Participants Who Achieved HSS7 = 0 (Controlled Disease) by Visit During the PC Period Using Observed Values	FAS
4.2.2.2	Kaplan-Meier Curve of the Time to First Achievement of HSS7 MID (≥ 5-Point) Improvement From Baseline Up to Week 36	FAS
[redacted]		
4.51.1.1	Box Plot of Mean (± SE) of Select Laboratory Values by Visit and Treatment Group	Safety
4.5.1.1.2	Box Plot of Mean (± SE) of Change From Baseline in Select Laboratory Values by Visit and Treatment Group	Safety
4.5.1.1.3	Box Plot of Mean (± SE) of Percent Change From Baseline in Select Laboratory Values by Visit and Treatment Group	Safety
4.5.1.2.1	Box Plot of Mean (± SE) of Select Laboratory Values by Visit and Treatment Group During the EXT Period	EXT-Evaluable
4.5.1.2.2	Box Plot of Mean (± SE) of Change From Baseline in Select Laboratory Values by Visit and Treatment Group During the EXT Period	EXT-Evaluable
4.5.1.2.3	Box Plot of Mean (± SE) of Percent Change From Baseline in Select Laboratory Values by Visit and Treatment Group During the EXT Period	EXT-Evaluable
4.5.2.1.1	Box Plot of Mean (± SE) of Lipid Panel Values by Visit and Treatment Group	Safety
4.5.2.1.2	Box Plot of Mean (± SE) of Change From Baseline of Lipid Panel Values by Visit and Treatment Group	Safety
4.5.2.1.3	Box Plot of Mean (± SE) of Percent Change From Baseline of Lipid Panel Values by Visit and Treatment Group	Safety
4.5.2.2.1	Box Plot of Mean (± SE) of Lipid Panel Values by Visit and Treatment Group During the EXT Period	EXT-Evaluable
4.5.2.2.2	Box Plot of Mean (± SE) of Change from Baseline in Lipid Panel Values by Visit and Treatment Group During the EXT Period	EXT-Evaluable

Figure No.	Title	Population
4.5.2.2.3	Box Plot of Mean (± SE) of Percent Change From Baseline of Lipid Values by Visit and Treatment Group During the EXT Period	EXT-Evaluable
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[redacted]	
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Listing No.	Title
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