STATISTICAL ANALYSIS PLAN

ABTECT-1 – ABX464 Treatment Evaluation for Ulcerative Colitis Therapy -1 (ABX464-105)

A randomized, double-blind, placebo-controlled, multicenter phase III study to evaluate the efficacy and safety of ABX464 once daily for induction treatment in subjects with moderately to severely active ulcerative colitis

AUTHOR: [redacted]

VERSION 2.0/15-Jul-2025

SIGNATURE PAGE

Statistical Analysis Plan V2.0/15-Jul-2025 for ABX464-105 Clinical Study Protocol V5.1.

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MODIFICATION HISTORY

Version	Date	Author	Summary of Significant Changes
1	27-Jun-2025	[redacted]	Not applicable (N/A) – first version
2	15-Jul-2025	[redacted]	Section 6.2 - Removed redundant description on baseline derivation. Section 7.4 - Removed “APPENDIX 4" from the second paragraph. Appendix 6 - Specified that histologic remission and/or histologic improvement can be derived if the grades defining the non-response criteria are present and all 0. - Added an example of deriving histologic remission and/or histologic improvement when Geboes Index Score is missing to Table J.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

Abbreviation or Term	Definition
AE	Adverse event
AESI	Adverse event of special interest
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
ANCOVA	Analysis of covariance
ASA	Aminosalicylic acid
AST	Aspartate aminotransferase
AT-IR	Inadequate response to advanced therapies
BMI	Body mass index
BU	Bowel urgency
CI	Confidence interval
CMH	Cochran Mantel Haenszel
CMQ	Custom MedDRA query
CTCAE	Common terminology criteria for adverse events
CS	Clinically significant
CSR	Clinical study report
ECG	Electrocardiogram
eCRF	Electronic case report form
e-Diary(ies)	Electronic diary(ies)
EIM	Extraintestinal manifestations
EMA	European Medicines Agency
EQ-5D-5L	European Quality of Life 5 Dimensions 5 Level
EU	European Union
FACIT	Functional assessment of chronic illness therapy
FAS	Full analysis set
FC	Fecal calprotectin
FCS	Fully conditional specification
FDA	Food and Drug Administration
[redacted]	[redacted]
HEMI	Histologic-endoscopic mucosal improvement
HEMR	Histologic-endoscopic mucosal remission
hsCRP	High-sensitivity C-reactive protein
IBDQ	Inflammatory bowel disease questionnaire
[redacted]	[redacted]
IDMC	Independent data monitoring committee
IE	Intercurrent event
INR	International normalized ratio
IRT	Interactive response technology
JAK	Janus kinase
LLQ	Lower limit of quantification
[redacted]	[redacted]
MAR	Missing at random
MCMC	Markov Chain Monte Carlo
MedDRA	Medical Dictionary for Regulatory Activities
MES	Mayo endoscopic subscore

Abbreviation or Term	Definition
miR-124	Micro-ribonucleic acid 124
MMRM	Mixed model for repeated measures
MMS	Modified Mayo Score
MNAR	Missing not at random
N/A	Not applicable
NBM	Nocturnal bowel movement
NCS	Not clinically significant
NRI	Non-responder imputation
NRS	Numeric rating scale
[redacted]	[redacted]
OR	Odds ratio
PD	Protocol deviation
PGA	Physician's global assessment
PK	Pharmacokinetics
pMMS	Partial Modified Mayo Score
PRO	Patient-reported outcome
PT	Preferred term
QD	Once daily
RB	Rectal bleeding
RBS	Rectal bleeding subscore
S1P	Sphingosine 1-phosphate
SAP	Statistical analysis plan
SD	Standard deviation
SF	Stool frequency
SFS	Stool frequency subscore
SI	International system of units
SOC	System organ class
TBL	Total bilirubin
TEAE	Treatment-emergent adverse event
TLF	Table, listing, and figure
TMS	Total Mayo Score
TNF	Tumor necrosis factor
UC	Ulcerative Colitis
ULN	Upper limit of normal
ULQ	Upper limit of quantification
[redacted]	[redacted]
WHO	World Health Organization
WPAI	Work Productivity and Activity Impairment questionnaire
β-hCG	Beta-human chorionic gonadotropin

1. INTRODUCTION

This Statistical Analysis Plan (SAP) describes the statistical analyses for the Clinical Study Protocol ABX464-105 Version 5.1, dated 10th April 2024 and entitled: "A randomized, double-blind, placebo-controlled, multicenter, phase III study to evaluate the efficacy and safety of ABX464 once daily (QD) for induction treatment in subjects with moderately to severely active ulcerative colitis." Details of the statistical analyses of the pharmacokinetic (PK) data (obefazimod [redacted] concentrations) (described in Section 9.6 of the Clinical Study Protocol) will be specified in a separate analysis plan.

This SAP will not be updated in case of administrative changes or amendments to the Clinical Study Protocol unless the changes impact the analysis.

2. STUDY OBJECTIVES AND ESTIMANDS

The primary and key secondary efficacy objectives are defined separately for a) the US Food and Drug Administration (FDA) and national Regulatory Authorities other than the European Medicines Agency (EMA) and b) the EMA.

2.1. Terms and Study Specific Definitions

Term (Abbreviation)	Study-Specific Definition
Baseline	The last non-missing assessment performed on or prior to the start of study treatment, unless stated otherwise
Bowel Urgency (BU)	A sudden, almost uncontrollable need to go to the toilet due to bowel movement
Clinical Remission	SFS=0 or 1, and RBS=0 and MES=0 or 1 (MES of 1 modified to exclude friability) *Note:* Symptomatic Remission is SFS=0 or 1 and RBS=0.
Clinical Response	A reduction from Baseline in MMS ≥2 points and a relative reduction from Baseline in MMS ≥30%, and a reduction from Baseline in RBS ≥1 point and/or RBS=0 or 1 *Note:* A Partial Clinical Response per pMMS is a reduction from Baseline in pMMS ≥1 points and a relative reduction from Baseline in pMMS ≥30%, and a reduction from Baseline in RBS ≥1 point and/or RBS=0 or 1
Endoscopic Improvement	MES=0 or 1 (MES of 1 modified to exclude friability)
Endoscopic Remission	MES=0
Extraintestinal Manifestations (EIM)	Ocular manifestations (uveitis, scleritis, episcleritis), rheumatological manifestations (axial spondyloarthritis, peripheral spondyloarthritis, arthralgia) or dermatological manifestations (psoriasis, pyoderma gangrenosum, erythema nodosum)
Fatigue Remission	A Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue subscale score >40
Histologic-endoscopic Mucosal Improvement (HEMI)	Endoscopic improvement associated with histologic improvement per Geboes scoring

Term (Abbreviation)	Study-Specific Definition
Histologic-endoscopic Mucosal Remission (HEMR)	Endoscopic remission associated with histologic remission per Geboes scoring
Histologic Improvement	A Geboes Index score ≤3.1
Histologic Remission	A Geboes Index score <2.0 (no neutrophils or eosinophils in lamina propria or in epithelium, no erosion, no ulceration)
Inflammatory Bowel Disease Questionnaire (IBDQ) Remission	A IBDQ total score ≥170
IBDQ Response	An increase of IBDQ total score ≥16 from Baseline
Modified Mayo Score (MMS)	The sum of 3 component scores: Rectal Bleeding Subscore (RBS), Stool Frequency Subscore (SFS) and Mayo Endoscopic subscore (MES) *Note:* The Partial Modified Mayo Score (pMMS) is a combination of RBS and SFS, and the Total Mayo Score (TMS) is the sum of 4 component scores: RBS, SFS, MES and Physician's Global Assessment subscore (PGA)
Nocturnal Bowel Movement (NBM)	One or more sleep interruptions due to a bowel movement
Symptomatic Remission	SFS=0 or 1 and RBS=0

2.2. Primary Efficacy Objectives and Endpoints

For the US FDA and national Regulatory Authorities other than the EMA, the primary efficacy objective is to compare the efficacy of obefazimod versus placebo on clinical remission, defined as the proportion of subjects in clinical remission at Week 8.

For the EMA, the primary efficacy objective is to compare the efficacy of obefazimod versus placebo on endoscopic improvement and symptomatic remission. The co-primary endpoints are defined as:

- Proportion of subjects who achieve endoscopic improvement at Week 8.
- Proportion of subjects with symptomatic remission at Week 8.

2.3. Key Secondary Efficacy Objectives and Endpoints

For the US FDA and national Regulatory Authorities other than EMA, the key secondary efficacy objectives and endpoints are ordered and described as follows:

- To compare the efficacy of obefazimod versus placebo on endoscopic improvement, defined as the proportion of subjects who achieve endoscopic improvement at Week 8.
- To compare the efficacy of obefazimod versus placebo on clinical response, defined as the proportion of subjects with clinical response at Week 8.
- To compare the efficacy of obefazimod versus placebo on HEMI, defined as the proportion of subjects with HEMI per Geboes scoring at Week 8.

For the EMA, the key secondary efficacy objectives and endpoints are ordered and described as follows:

- To compare the efficacy of obefazimod versus placebo on clinical remission, defined as the proportion of subjects who achieve clinical remission at Week 8.
- To compare the efficacy of obefazimod versus placebo on clinical response, defined as the proportion of subjects with clinical response at Week 8.

- To compare the efficacy of obefazimod versus placebo on HEMI, defined as the proportion of subjects with HEMI per Geboes scoring at Week 8.

2.4. Other Secondary Efficacy Objectives and Endpoints

Other secondary efficacy objectives and endpoints are:

- To compare the efficacy of obefazimod versus placebo on MMS, defined as the change from Baseline in MMS at Week 8.
- To compare the efficacy of obefazimod versus placebo on pMMS, defined as the change from Baseline in pMMS by visit.
- To compare the efficacy of obefazimod versus placebo on partial clinical response, defined by the proportion of subjects with partial clinical response by visit.
- To compare the efficacy of obefazimod versus placebo on symptomatic remission, defined by the proportion of subjects with symptomatic remission by visit.
- To compare the efficacy of obefazimod versus placebo on RBS, defined by the:
  - Proportion of subjects with RBS=0 by visit.
  - Proportion of subjects with ≥1 point improvement from Baseline in RBS by visit.
  - Change from Baseline in RBS by visit.
- To compare the efficacy of obefazimod versus placebo on SFS, defined by the:
  - Proportion of subjects with SFS=0 or 1 by visit.
  - Proportion of subjects with ≥1 point improvement from Baseline in SFS by visit.
  - Change from Baseline in SFS by visit.
- To compare the efficacy of obefazimod versus placebo on BU, defined by the proportion of subjects with BU=0 by visit in the subpopulation of subjects with BU at Baseline.
- To compare the efficacy of obefazimod versus placebo on Fecal Calprotectin (FC), defined by:
  - Change from Baseline in FC by visit.
  - Proportion of subjects with FC below 150 µg/g by visit.
- To compare the efficacy of obefazimod versus placebo on Fatigue Numeric Rating Scales (NRS), defined by the change from Baseline in the fatigue NRS by visit.
- To compare the efficacy of obefazimod versus placebo on FACIT-Fatigue questionnaire, defined by the change from Baseline in the FACIT-Fatigue at Week 8.
- To compare the efficacy of obefazimod versus placebo on histologic improvement, defined by the proportion of subjects who achieve histologic improvement per Geboes scoring at Week 8.
- To compare the efficacy of obefazimod versus placebo on endoscopic remission, defined by the proportion of subjects who achieve endoscopic remission at Week 8.
- To compare the efficacy of obefazimod versus placebo on HEMR, defined by the proportion of subjects with HEMR per Geboes scoring at Week 8.
- To compare the efficacy of obefazimod versus placebo on histologic remission, defined by the proportion of subjects who achieve histologic remission per Geboes scoring at Week 8.
- To compare the efficacy of obefazimod versus placebo on IBDQ, defined by the:
  - Change from Baseline in IBDQ total score and domain subscores at Week 8.
  - Proportion of subjects with IBDQ response at Week 8.
- To compare the efficacy of obefazimod versus placebo on NBM, defined by the proportion of subjects with no NBM by visit in the sub-population of subjects with NBM at Baseline.
- To compare the efficacy of obefazimod versus placebo on EIM, defined by the

proportion of subjects with no EIM at Week 8 in the subpopulation of subjects having EIM at the Baseline visit.

- To compare the efficacy of obefazimod versus placebo on European Quality of Life 5 Dimensions 5 Level (EQ-5D-5L) questionnaire, defined by the change from Baseline in EQ-5D-5L index score by visit.
- To compare the efficacy of obefazimod versus placebo on High-sensitivity C-Reactive Protein (hsCRP), defined by the change from Baseline in hsCRP by visit.
- To compare the efficacy of obefazimod versus placebo in Work Productivity and Activity Impairment questionnaire (WPAI), defined by the change from Baseline in WPAI: Ulcerative Colitis (UC) score at Week 8.
- To compare the efficacy of obefazimod versus placebo on any UC-related health care encounters, defined by the proportion of subjects with UC-related health care encounters.
- To compare the effect of obefazimod versus placebo on Micro-ribonucleic Acid 124 (miR-124) expression in tissue and in blood, defined by the change from Baseline in miR-124 expression in rectal/sigmoidal biopsies at Week 8 and in blood by visit.
- To compare the effect of obefazimod versus placebo on proinflammatory cytokine plasma concentrations, defined by the:
  - Change from Baseline in proinflammatory cytokine plasma concentrations by visit.
  - Change from Baseline in proinflammatory cytokine plasma concentrations by visit in the subgroup of subjects with clinical remission and clinical responders.
- To assess the concentration of obefazimod and its [redacted] after oral administration, defined by the plasma concentrations of obefazimod and [redacted] at Baseline, Week 4 and Week 8 (at specified time points depending on the group allocated via Interactive Response Technology (IRT)).

2.5. Safety Objectives

Safety objectives and endpoints are to evaluate the safety profile of obefazimod versus placebo during induction, defined by:

- Incidence of all Treatment-emergent Adverse Events (TEAEs), causally-related TEAEs, all serious TEAEs and causally-related serious TEAEs classified by severity.
- Incidence of TEAEs leading to investigational product discontinuation and study discontinuation.
- Incidence of treatment-emergent adverse events of special interest (AESIs).
- Incidence of clinically significant laboratory abnormalities.
- Incidence of clinically significant abnormalities regarding vital signs and electrocardiograms (ECGs).

2.5.1. [redacted]

2.6. Estimands

Table A describes primary and key secondary estimands' attributes to support regulatory decisions.

Table A: Estimands

Regulatory Authority	Estimand	Definition	Attributes					
			Treatment	Population	Variable/Endpoint	Intercurrent Events (IEs)	IE Handling Strategy	Population-Level Summary Measure
US FDA and national Regulatory Authorities other than EMA	Primary Estimand	Clinical Remission at Week 8	Obefazimod 50 mg QD or Obefazimod 25 mg QD or Placebo	Subjects with moderate to severe active UC who receive at least one dose of study treatment	Proportion of subjects with Clinical Remission at Week 8	[redacted]	Composite Strategy: [redacted]	Common risk difference in proportions and odds ratio (OR) between treatment groups (i.e., obefazimod 50 mg QD or 25 mg QD versus placebo) and their associated confidence intervals (CIs)
	Key Secondary Estimand 1	Endoscopic Improvement at Week 8	As per Primary Estimand		Proportion of subjects with Endoscopic Improvement at Week 8	As per Primary Estimand		
	Key Secondary Estimand 2	Clinical Response at Week 8	As per Primary Estimand		Proportion of subjects with Clinical Response at Week 8	As per Primary Estimand		
	Key Secondary Estimand 3	HEMI per Geboes scoring at Week 8	As per Primary Estimand		Proportion of subjects with HEMI per Geboes scoring at Week 8	As per Primary Estimand		

Regulatory Authority	Estimand	Definition	Attributes					
			Treatment	Population	Variable/Endpoint	Intercurrent Events (IEs)	IE Handling Strategy	Population-Level Summary Measure
EMA	Primary Estimand 1	Endoscopic Improvement at Week 8	Obefazimod 50 mg QD or Obefazimod 25 mg or Placebo	Subjects with moderate to severe active UC who receive at least one dose of study treatment	Proportion of subjects with Endoscopic Improvement at Week 8	[redacted]	Composite Strategy: [redacted]	Common risk difference in proportions and OR between treatment groups (i.e., obefazimod 50 mg QD or 25 mg QD versus placebo) and their associated CIs)
	Primary Estimand 2	Symptomatic Remission at Week 8	As per Primary Estimand 1		Proportion of subjects with Symptomatic Remission at Week 8	As per Primary Estimand 1		
	Key Secondary Estimand 1	Clinical Remission at Week 8	As per Primary Estimand 1		Proportion of subjects with Clinical Remission at Week 8	As per Primary Estimand 1		
	Key Secondary Estimand 2	Clinical Response at Week 8	As per Primary Estimand 1		Proportion of subjects with Clinical Response at Week 8	As per Primary Estimand 1		

Regulatory Authority	Estimand	Definition	Attributes					
			Treatment	Population	Variable/Endpoint	Intercurrent Events (IEs)	IE Handling Strategy	Population-Level Summary Measure
	Key Secondary Estimand 3	HEMI per Geboes scoring at Week 8	As per Primary Estimand 1		Proportion of subjects with HEMI per Geboes scoring at Week 8	As per Primary Estimand 1		

3. STUDY DESIGN

This is a multicenter, randomized, placebo-controlled study to evaluate the efficacy and safety of obefazimod given at 25 or 50 mg QD in subjects with moderately to severely active UC who have inadequate response (lack of response, loss of response, intolerance) to either conventional therapies and/or advanced therapies.

3.1. General Description

As shown below, this study consists of a screening period of up to 28 days, an 8-week induction period, followed by a 28-day follow-up period (for subjects who do not continue in the maintenance study (i.e., ABX464-107).

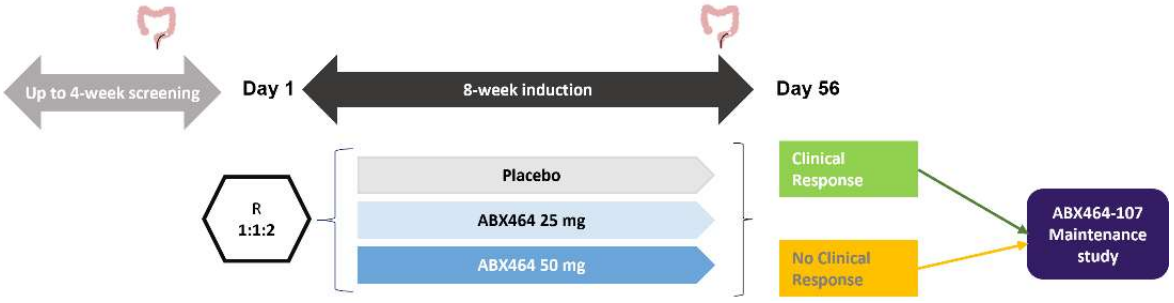
Subjects who complete the 8-week induction period will be given the opportunity to take part in the maintenance study (i.e., ABX464-107), either:

- In the randomized double-blind placebo-controlled study part (Part 1: placebo, obefazimod 25 mg, obefazimod 50 mg) for clinical responders at Week 8.
- In the randomized study part (Part 2: obefazimod 25 mg or obefazimod 50 mg) for clinical non-responders at Week 8.

Approximately 612 subjects will be randomized in this induction study. On Day 1 of the induction study, eligible subjects will be randomized and allocated into three treatment arms according to ratio 1:1:2 as follows:

- Placebo: 153 subjects
- Obefazimod – Daily dose 25 mg QD: 153 subjects
- Obefazimod – Daily dose 50 mg QD: 306 subjects

Figure 1: Study Design



Randomization will be stratified according to the following factors:

- Inadequate response (lack of response, loss of response, or intolerance) to advanced therapies (AT-IR) (Yes/No)
- Baseline oral corticosteroid use (Yes/No)

At Day 56, subjects [redacted] to either take part in the maintenance study (i.e., ABX464-107) or to end their participation in the present induction study by completing the study. For the latter option, subjects will return for an end of study visit 28 days after the last study drug intake. Subjects will be evaluated for safety and efficacy throughout the induction study.

Electronic diaries (e-Diaries) will be used to collect the following on a daily basis: SF, RB, NBUs, BU, fatigue NRS, study medication taken (Yes/No) and study medication intake time. [redacted]

3.2. Sample Size Determination

3.2.1. Global Study

Sample size calculations are performed with nQuery, version 7 or higher.

Primary Endpoint (US FDA and national Regulatory Authorities other than the EMA):

Taking into consideration the impact of the strategy to handle IEs, a total of 612 subjects will allow the detection of a difference [redacted] This calculation is based on a Chi-square test with a type I [redacted] two-sided) and assumes a placebo clinical remission rate [redacted] (see APPENDIX 1 nQuery Calculation 1). This sample size also provides [redacted] power to detect the same treatment difference between obefazimod 25 mg and placebo, with the same assumptions, except using a type I [redacted] (according to the multiplicity adjustment procedure) (see APPENDIX 1 nQuery Calculation 2). This sample size will also allow the detection of a difference of at least [redacted] in the clinical remission rate at Week 8 among subjects with AT-IR [redacted] between obefazimod 50 mg and placebo with a statistical power of at least [redacted] (see APPENDIX 1 nQuery Calculation 3). Differences of [redacted] were also evaluated, and the associated powers are [redacted] respectively. These calculations are based on a Chi-square test with a type I [redacted] two-sided) and assumes a placebo clinical remission rate of [redacted] (see APPENDIX 1 nQuery Calculations 4 and 5).

Co-primary Endpoints (EMA):

A statistical power calculation for co-primary endpoints according to European Union (EU) EMA guidance is also performed. The calculation for each of the co-primary endpoints is based on a Chi-square test with a type I [redacted] two-sided.

- Endoscopic Improvement:
  A total of 612 subjects will provide [redacted] power to detect a [redacted] difference between obefazimod 50 mg and placebo in the endoscopic improvement rate at Week 8, assuming a placebo rate of [redacted] and a type I [redacted] (see APPENDIX 1 nQuery Calculation 6) . This sample size also provides at least [redacted] power to detect the same treatment difference between obefazimod 25 mg and placebo, with the same assumptions, except using a type I [redacted] (according to the multiplicity adjustment procedure) (see APPENDIX 1 nQuery Calculation 7).

- Symptomatic Remission:
  A total of 612 subjects will provide [redacted] power to detect a [redacted] difference between obefazimod 50 mg and placebo in the symptomatic remission rate at Week 8, assuming a placebo rate of [redacted] and a type I error rate of [redacted] (see APPENDIX 1 nQuery Calculation 8). This sample size also provides at least [redacted] power to

detect the same treatment difference between obefazimod 25 mg and placebo, with the same assumptions, except using a type I error rate of [redacted] (according to the multiplicity adjustment procedure) (see APPENDIX 1 nQuery Calculation 9).

Considering the clinical hypotheses described above for the co-primary endpoints of endoscopic improvement and symptomatic remission, the statistical power to detect clinically relevant differences for both co-primary endpoints is [redacted] for the comparison between obefazimod 50 mg and placebo and [redacted] for the comparison between obefazimod 25 mg and placebo. This calculation assumes that there is no correlation between endoscopic improvement and symptomatic remission. The statistical power will be even higher considering these two outcomes are likely positively correlated.

3.2.2. [redacted]

[redacted]

3.3. Schedule of Events

A schedule of events can be found in Section 5.1 Schedule of Assessments of the Clinical Study Protocol.

3.4. Changes to Analysis from Clinical Study Protocol

Any analyses described in this SAP that differ from the details provided in the Clinical Study Protocol are listed below:

- The following are considered 'other secondary endpoints' or 'exploratory endpoints' per this SAP, though these are not included in the Clinical Study Protocol:
  - Proportion of subjects with ≥1 point improvement from Baseline RBS by visit.
  - Change from Baseline in RBS by visit.
  - Proportion of subjects with ≥1 point improvement from Baseline SFS by visit.
  - Change from Baseline in SFS by visit.
  - Proportion of subjects with Fatigue remission.
  - Proportion of subjects with IBDQ remission.
  - Change from Baseline in proinflammatory cytokine plasma concentrations by visit in the subgroup of subjects with clinical remission and clinical responders.
- Additional sensitivity analyses of the primary and key secondary estimands is described in Section 17.1.4 (Sensitivity Analyses #3 and #4) of this SAP. These sensitivity analyses are not mentioned in the Clinical Study Protocol.
- [redacted]
- This SAP refers to UC-related health care encounters, whereas the Clinical Study Protocol refers to UC-related visits to the emergency room, hospitalization or surgery. The SAP language has been used to more closely align with the wording/labeling used

on the corresponding electronic Case Report Form (eCRF) page.

- Clinical Study Protocol Section 9.3.3 references the individual IBDQ bowel symptom domain items (questions) as an other secondary efficacy continuous endpoint. An analysis of these individual items responses is not required hence, this endpoint has not been included in this SAP.
- Clinical Study Protocol Sections 5.3.7.2 and 5.3.7.3 specify that BU and NBM will be calculated using three consecutive days prior to each visit.

[redacted]

4. PLANNED ANALYSES

A quarterly summarization of relevant study data for review by an Independent Data Monitoring Committee (IDMC) as well as a Final Analysis will be performed for this study.

4.1. Independent Data Monitoring Committee (IDMC)

A separate, unblinded Biostatistics and Programming team will be assigned to produce the unblinded summaries required for quarterly IDMC review. This unblinded team will be separate from the operational blinded Biostatistics and Programming team.

Note: This SAP does not describe planned IDMC summaries, nor the unblinding process. These are described in the IDMC Charter, Unblinded Data Plan/Data transfer specification, DMC Analysis Plan, and IDMC Table, Listing, and Figure (TLF) shells documents.

4.2. Interim Analysis

No interim analysis is planned.

4.3. Final Analysis

All final, planned analyses identified in this SAP will be performed by [redacted] following Sponsor authorization of this SAP, Database Lock, and Unblinding of Treatment.

5. ANALYSIS SETS

Agreement and authorization of subjects included/excluded from each analysis set will be conducted prior to the unblinding of the study:

- The **Screened Set** includes all subjects who signed informed consent.
- The **Randomized Set** includes all subjects who were randomized to study treatment.
- The **FAS** includes all randomized subjects who received at least one dose of study drug. Subjects will be analyzed according to the treatment group to which they were randomized (i.e., “as randomized”), regardless of the treatment received. The efficacy analysis will be based on the FAS.
- The **Safety Set** includes all randomized subjects who have received at least one dose of study drug. Subjects will be analyzed according to the treatment received (i.e., “as treated”). Subjects who receive a different dose other than what they were randomized to, will be

grouped according to the most frequently received dose. When both doses possess an equivalent duration, the higher dosage will be used. The safety analysis will be based on the Safety Set, unless specified otherwise.

- [redacted]
- The **PK Set** will include [redacted] who received at least one dose of obefazimod and have at least one quantifiable post-dose obefazimod [redacted] concentration.

6. GENERAL CONSIDERATIONS

6.1. Reference Start Date and Study Day

Study Day will be calculated from the reference start date and will be used to show start/stop day of assessments and events. Reference start date is defined as the date of first dose (Day 1). Study Day will appear in every listing where an assessment date or event date appears.

If the date of the event is on or after the reference start date, then: Study Day = (date of event– reference start date) +1

If the date of the event is prior to the reference start date, then: Study Day = (date of event– reference start date).

In the case that the event date is partial or missing, Study Day and any corresponding durations will appear missing in the listings.

6.2. Baseline

Unless otherwise specified, Baseline is defined as the last non-missing measurement (including unscheduled assessments) taken on or prior to the start of study treatment. ECG assessments, vital sign assessments, and Patient-reported Outcomes (PRO) recorded on the same day as the first dose date will be considered Baseline regardless of the time of the assessment.

The time of first dose of study drug will be obtained from the PHARMACOKINETICS CONCENTRATION eCRF page, where the date of study drug administration matches the earliest start date of medication on the EXPOSURE eCRF page. If there is no record on the PHARMACOKINETICS CONCENTRATION eCRF page, where the date of study drug administration aligns with the earliest start date of medication on the EXPOSURE eCRF page, the time of first dose will be considered missing.

AEs and medications commencing on the reference start date (date of first dose of study drug) will be considered post-Baseline unless otherwise indicated based on available start date/time combination or collected eCRF information that identifies the individual event/medication as starting prior to first study drug administration (i.e., laboratory-related AEs – see Section 18.1.1 for more details).

[redacted]

[redacted]

6.3. Re-tests, Unscheduled Visits and Early Termination Data

For by-visit analyses and summaries, efficacy, safety, PRO and PK data (including scheduled, re-tests, unscheduled, and early termination) will be assigned to analysis visits after the application of the windowing conventions described in Section 6.4. All on-treatment measurements will be considered in summaries of abnormalities or worst-case values post-Baseline. The visit windowing will be applied before missing data are imputed. Listings will include scheduled, unscheduled, re-test, and early termination data.

6.4. Windowing Conventions

All scheduled study visits are defined relative to Study Day 1, the date of first dose. Clinical Study Protocol Section 5.1 defines the scheduled visit windows. A windowing convention will be used to determine the analysis visit value for a given measurement and will be applicable for all by-visit summaries and analyses for efficacy and safety data. Analysis visit windows are wider than the scheduled visit windows in the Clinical Study Protocol and are described in Table B.

Table B: Visit Windows for Safety and Efficacy Analyses

Safety Data	
Scheduled Visit (Protocol Scheduled Day)	**Analysis Visit Window (Study Day)**
Baseline	Derived in accordance with details in Section 6.2
Week 4 (Day 28)	2-42
Week 8 (Day 56)	43-70
Safety Follow-up (Day 84)	>5 days after the last dose–35 days after the last dose*
Efficacy and PK Data	
Scheduled Visit (Protocol Scheduled Day)	**Analysis Visit Window (Study Day)**
Baseline	Derived in accordance with details in Section 6.2
Day 1	1**
Week 4 (Day 28)	21-35
Week 8 (Day 56)	43-70

**If the assessment was performed ≤5 days after the last dose, the assessment will be mapped to the visit in the window where it occurred.*

***Relevant for PK assessments on Day 1 only. Windowing will be applied prior to any missing data imputations. Unless stated otherwise, data from all visits including scheduled, unscheduled, early termination, and safety follow-up visits will be eligible for allocation to an analysis visit.*

The last non-missing measurement taken on or prior to Day 1 (including unscheduled assessments) will be labelled as "Baseline" in accordance with the details specified in Section 6.2.

The latest post-Baseline non-missing measurement taken on or before the date of last dose of study drug will be labelled as the 'End of Treatment' value.

If one or more results for a variable are assigned to the same analysis visit, the result with the date closest to the Clinical Study Protocol scheduled day (or the latest result in the case of data assigned to Screening) will be used in the analysis. Component subscores of all composite scores (e.g., MMS, pMMS, TMS) from the same date will be used in the analysis. Similarly, for

composite endpoints (such as clinical remission), the component scores from the same date will be used in the analysis.

If two measurements in the same analysis visit window are equidistant from the Clinical Study Protocol scheduled study day, the earliest measurement will be used in the analysis. If multiple assessments are available on the same day, then the average of the assessment (or worst outcome, for categorical data) will be used in the analysis, except for laboratory, ECG and eDiary data where the assessment at the latest time of the same day will be used. For laboratory assessments, if multiple quantitative results are available on the same date/time for the same parameter, then the average of the results will be used in the change from Baseline analyses.

Notes:

- By-visit summaries and analyses (including Mixed Model for Repeated Measures (MMRM) analyses) will include only those visits where the assessment in question was scheduled to occur. [redacted]
- Per the details provided in Section 17.4, selected daily diary items will be summarized by week. The derivation of weekly scores for these items will be performed independent of the visit windowing methods outlined above. See Section 17.4 for details.
- Laboratory-related efficacy data (such as FC, hsCRP and cytokines) are considered in the efficacy visit windows for mapping to an analysis visit.

6.5. Statistical Tests

The default significance level will be 0.05, level of CIs will be 95%, and all tests will be performed 2-sided, unless specified otherwise.

6.6. Common Calculations

For quantitative measurements:

- Change from Baseline = Value at Visit X–Baseline value
- Percent change from Baseline = (Value at Visit X–Baseline value)/Baseline value*100

6.7. Software Version

All analyses will be conducted using [redacted]

7. STATISTICAL CONSIDERATIONS

7.1. Adjustments for Covariates and Factors to be Included in Analyses

The following factors (i.e., the randomization strata), and/or endpoint Baseline measure will be used in the analyses. For details of their inclusion in the models, refer to the specific analysis section.

- Inadequate response to advanced therapies (AT-IR) (Yes/No)
- Baseline oral corticosteroid use (Yes/No)

Note: The values used for the above factors will be those entered in the IRT system at randomization.

7.2. Multicenter Studies

This study will be conducted by multiple investigators at multiple centers internationally. Data from all sites will be pooled and statistical analyses will not be adjusted per investigational site.

7.3. Intercurrent Events (IEs)

In this section, mechanisms for identifying potential IEs related to the primary and key secondary estimands are described and policies for handling these are defined.

The Composite Strategy will be applied for each of the above IEs for the main analyses of all primary and key secondary estimands. This same approach will be used for the sensitivity analyses of the primary and key secondary estimands. For each of these analyses, IEs will be handled as described in Section 17.

For the supplementary analysis of all primary and key secondary estimands, a Treatment Policy approach will be applied for the above three IEs. For these analyses, the IEs are considered irrelevant; the data are analyzed irrespective the occurrence of any IEs. More details on this analysis are provided in Section 17.1.5.

While an estimands framework is not applied to the other secondary efficacy endpoints, subjects with any of the above IEs occurring before the relevant efficacy assessment will be treated as non-responders in the analysis of categorical other secondary efficacy variables, and assessments occurring after the above IEs will be considered missing in the analysis of continuous other secondary efficacy variables.

A listing of subjects experiencing any IE will be presented. If a subject satisfies more than one IE, each event will be displayed.

7.4. Missing Data

In the main analysis of all binary responder-type endpoints, subjects with missing data, regardless of reason for missingness, will be considered as non-responders. In the analysis of continuous or score endpoints, missing continuous outcome data will not be imputed for Analysis of Covariance (ANCOVA). However, they will be handled by implicit imputation in the MMRM analysis under MAR assumption. Sensitivity analyses will be performed for the primary and key secondary efficacy endpoints, where multiple imputation methods will be used to address missing data. These are described in Section 17.1.4. Section 17.4 includes details on how missing diary data will be handled for exploratory analyses.

Missing AE relationship to study treatment will be imputed as described in Section 18.1. Partial or missing AE start dates, concomitant medication start dates will be imputed as described in APPENDIX 2 to assist with a) the derivation of exposure-adjusted incidence rates for AEs and b) defining events as treatment-emergent or medications as prior/concomitant. Partial date of UC diagnosis will also be imputed as described in APPENDIX 2, to enable the derivation of duration of UC.

No other safety data will be imputed.

7.5. Multiple Comparisons/Multiplicity

[redacted]

[redacted]

[redacted]

[redacted]

7.6. Examination of Subgroups

The following subgroup analyses will be conducted [redacted] in the FAS.

- Sex (Male/Female)
- Age (≤median/>median), (<65/≥65)
- Race – subjects with 'unknown' or 'not reported' race will be excluded, subjects with more than one race recorded will be summarized under 'Multiple'
- Ethnicity (Hispanic or Latino/not Hispanic or Latino)
- Inadequate response to advanced therapies (AT-IR)* (Yes/No)
- Number of prior AT-IR by medication name (1, 2, 3, 4+)**
- Number of prior AT-IR by medication type (1, 2, 3, 4+)
- Inadequate response (IR) to Janus kinase (JAK) inhibitors among subjects with AT-IR (Yes/No)
- Number of non-JAK inhibitor AT-IR among subjects who have IR to JAK inhibitors (0/1+)
- Baseline oral corticosteroids use* (Yes/No)
- Baseline MMS (≤7/>7)
- Extent of disease at Baseline per Investigator (proctitis (<15cm from anal verge, proctosigmoiditis (≥15cm from anal verge), left-sided colitis, extensive colitis)
- Duration of UC (≤median/median)
- Baseline hsCRP (≤median/>median)
- Baseline FC (≤median/>median)
- Region (China/non-China; North America, Western Europe, Eastern Europe, China,

Rest of World)
- Current Tobacco Use (Yes/No)

*__Baseline oral corticosteroid use__ (Yes/No) use and __AT-IR__ (Yes/No) will be based upon eCRF data (rather than IRT randomization strata). Further details are discussed in Section 9.2.
**Brand name(s) and generic name of the same medication will be considered one medication, dose adjustment of the same medication will be considered one medication, biosimilar(s) will be considered the same medication as initially marketed one.

Subjects with **inadequate response to JAK inhibitor** will be considered those who have at least one entry on the PRIOR THERAPIES FOR UC eCRF with Medication Type = JAK inhibitors and 'Has the subject failed to this therapy?' = Yes, and reason(s) for failure includes at least one of the following: lack of response, loss of response or intolerance.

The **number of prior AT-IR by medication name** will be the number of distinct AT-IR medication preferred names/drug codes, per subject. Biosimilar medications may have different preferred names/drug codes; these will be identified by a blinded data review and will be included with the marketed medication name.

The **number of prior AT-IR by medication type** will be the number of distinct AT-IR medication types (as captured on PRIOR THERAPIES FOR UC eCRF page), per subject. Medications with preferred term (PT) code '06257601001' (e.g. Stelara, Ustekinumab) will be re-mapped to medication type = Anti-IL12/23 for summaries.

Current tobacco use will be based on the SUBSTANCE USAGE eCRF. Subjects will be considered "yes" if data collected is "current" use and "no" if data collected is "former" or "never".

Additional subgroups may be assessed, if deemed necessary. The medians will be derived based on the FAS from all treatment groups pooled. It should be noted that the study was not designed to detect treatment differences with high statistical power within subgroups. If any subgroup includes <5% of all subjects, no inferential statistics will be generated. However, descriptive statistics for the subgroup will still be presented.

8. OUTPUT PRESENTATIONS

For continuous variables, descriptive summary statistics will include n (number of subjects), mean, SD, median, minimum, and maximum.

For categorical variables, descriptive summary statistics will include n and percent.

APPENDIX 3 shows the conventions for presentation of data in outputs.

9. DISPOSITION AND WITHDRAWALS

9.1. Disposition

A summary of subject disposition will be provided for the Screened Set, using randomized treatment, where the number of subjects in each of the following categories will be summarized

by treatment group and overall (Total):

- Subjects screened (Total only)
- Screen failures (includes both subjects who failed screening and subjects who discontinued prior to randomization)
- Subjects randomized
- Subjects randomized but not dosed
- Subjects who took at least one dose of study drug
- Subjects who completed full course of study treatment
- Subjects who prematurely discontinued study drug, overall and by reason for discontinuation
- Subjects who completed the study
- Subjects who prematurely discontinued from study, overall and by reason for discontinuation
- Subjects continuing into the maintenance study (i.e., ABX464-107)

All reasons for discontinuation will be displayed in the summary, even if the count is zero.

Note: The number of randomized subjects will be used as the denominator for the calculation of percentages for all except a) the number of subjects screened (where only counts will be displayed), b) the number of subjects who failed screening (where the denominator will be the number of subjects screened) and c) reasons for study drug discontinuation and reasons for study discontinuation (where the denominator will be the number of subjects who discontinued study drug and discontinued the study, respectively).

Disposition data will also be listed. The listing will include the previous subject number for subjects who were re-screened. Reason for failing previous screening will not be listed.
The number and percentage of subjects in each analysis set will be summarized, by treatment group and overall, for the Randomized Set. Subjects will be summarized by randomized treatment for all analysis sets, except for Safety Set, where actual treatment will be used. This information will also be listed.

A listing of subjects for who were unblinded during the study will be provided.

Details of any inclusion/exclusion criteria which were not met (per the INCLUSION/EXCLUSION CRITERIA eCRF page) will be listed for the Screened Set. Additionally, details of the Clinical Study Protocol version(s) under which each subject was consented and reconsented, will be included in a listing.

9.2. Randomization

The number and percentage of subjects per IRT randomization strata (i.e., AT-IR (Yes/No) and Baseline oral corticosteroids use (Yes/No) as reported by the investigators in IRT) will be presented for the FAS. This table will also include the number and percentage of subjects per strata based on eCRF data, the difference between the two (i.e., the number and percentage of subjects included in each IRT randomization stratum but NOT included in the corresponding stratum per eCRF data), and the overall summary per treatment of subjects who were mis-stratified to any of the strata.

The following methods will be used to determine each subject's strata per eCRF data:

- AT-IR: Subjects will be considered to have had AT-IR if they have at least one record

on the PRIOR THERAPIES FOR ULCERATIVE COLITIS eCRF page, where the Medication Type is marked as either Anti-Tumor Necrosis Factor (TNF), Anti-integrins, Anti-IL23, JAK inhibitor or Sphingosine 1-phosphate S1P receptor modulators **and** the question "Has the subject failed this therapy?" = Yes **and** the corresponding reason(s) for failure includes at least one of the following: lack of response, loss of response or intolerance.

- Baseline oral corticosteroids use: Subjects will be considered to have concomitant oral corticosteroids at Baseline if they have at least one record on the PRIOR AND CONCOMITANT MEDICATIONS eCRF page where ATC level 4 code is A07EA or H02AB, Route = Oral, the medication start date falls on or before the date of first dose of study treatment or is missing, and the medication end date falls on or after the date of first dose of study treatment or is missing or the medication is marked as Ongoing.

Randomization stratification data (per IRT and per eCRF) will also be listed. Subjects who were mis-stratified will be flagged.

9.3. Clinical Study Protocol Deviations (PDs)

Clinical Study Protocol Deviations (PDs) will be reviewed by the cross-functional Abivax and IQVIA teams on a regular basis during the study.

Important PDs are a subset of PDs that may significantly affect the completeness, accuracy, and/or reliability of the study data or that may significantly affect a subject's rights, safety, or well-being. Important PDs will be identified and agreed during the PD reviews and finalized prior to unblinding. Important PDs will be descriptively summarized by the following PD categories for the FAS:

- Informed Consent and Process
- Inclusion Criteria
- Exclusion Criteria
- Concomitant Medication
- Laboratory Assessment
- Study Procedures (not safety and efficacy related)
- Safety
- Randomization
- Visit Schedule
- Investigational Product Conditions
- Investigational Product Preparation
- Investigational Product Administration
- Subject Investigational Product Compliance
- Efficacy
- Subject Discontinuation
- Administrative
- Blinding
- Patient Reported Outcomes
- PK/PD
- Other Criteria

All PD categories will be displayed in the summary, even if the count is zero. PD categories will be listed by descending frequency in the Total column, then by descending frequency in the

obefazimod 50 mg column, then by descending frequency in the obefazimod 25 mg column, and then alphabetically in the event of a tie.

The following important PD impacting PK analyses will be programmed and summarized under the “PK/PD” category:

All PDs will be listed, and programmed PDs will be flagged.

10. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographic data and other Baseline characteristics will be presented for the FAS. The following variables will be summarized:

- Age at screening (years) – both as a continuous variable and frequency counts for each of the following groups:
  - <18 years, ≥18 years to <40 years, ≥40 years to <65 years, ≥65 years
  - ≤median, >median
- Sex (Male/Female)
- Women of child-bearing potential (Yes/No)
- Ethnicity (Hispanic or Latino/not Hispanic or Latino)
- Race (American Indian or Alaska Native, Asian (with a sub-category for Chinese), Black or African American, Native Hawaiian or Other Pacific Islander, White, Multiple, Not Reported, Unknown)
- Baseline height (cm)
- Baseline weight (kg)
- Baseline body mass index (BMI) (derived using: weight (kg)/height $(m)^2$)
- Region (North America, Western Europe, Eastern Europe, China, Rest of World)
- Tobacco user (Current, Former, Never)
- [redacted]

Baseline characteristics related to UC will also be summarized for the FAS. The following variables will be displayed:

- Duration of UC (years): derived using (date of informed consent–date of UC diagnosis (imputed where necessary))/365.25, summarized both as a continuous variable and frequency counts for the following groups: ≤median, >median
- Extent of disease per investigator (proctitis (<15cm from anal verge), proctosigmoiditis (≥15cm from anal verge), left-sided colitis, extensive colitis) – based on ENDOSCOPY eCRF page at Screening visit (if non-missing), otherwise based on ULCERATIVE COLITIS DISEASE HISTORY eCRF page
- Surgeries related to ulcerative colitis (Yes/No) and surgery types (Proctocolectomy, Partial Colectomy, Current Stoma, Other)
- IR to JAK inhibitors among subjects with AT-IR (Yes/No)
- Number of non-JAK inhibitor AT-IR among subjects who have IR to JAK inhibitors (0/1+)
- Number of prior AT-IR by medication name (0, 1, 2, 3, 4+)
- Number of prior AT-IR by medication type (0, 1, 2, 3, 4+) (with PT code = '06257601001' (e.g., Stelara, Ustekinumab) re-mapped to medication type = Anti-IL12/23)
- IR to prior medications of interest (Anti-TNF only, Vedolizumab only, Anti-TNF+Anti-integrin (Anti-TNF+Vedolizumab), Anti-TNF+Anti-integrin+Anti-interleukin (Anti-TNF+Vedolizumab+Ustekinumab))
- Baseline MMS – both as a continuous variable and frequency counts for the following groups: ≤7, >7
- Baseline TMS (as a continuous variable) and its components (SFS, RBS, MES and

PGA) summarized by frequency counts for the following levels: 0, 1, 2, 3 for SFS and PGA; 1, 2, 3 for RBS; 2, 3 for MES
- Baseline pMMS
- Baseline NBM – both as a continuous variable and frequency counts for the following groups: NBM=0, NBM>0 – see Section 17.3.1 for derivation details
- Baseline BU – both as a continuous variable and frequency counts for the following groups: BU=0, BU>0 – see Section 17.3.1 for derivation details
- Baseline hsCRP (mg/L) – both as a continuous variable and frequency counts for the following groups: ≤median, >median
- Baseline FC (µg/g) – both as a continuous variable and frequency counts for the following groups: ≤median, >median, <150, ≥150, and <250, ≥250
- Baseline EIM (None/At Least One) and type (Ocular, Axial Spondyloarthritis, Peripheral Spondyloarthritis, Arthralgia, Psoriasis, Pyoderma Gangrenosum, Erythema Nodosum)

Any median value will be based on all subjects in the FAS. The actual median value will be included as part of the subgroup label (e.g., ≤median (38.6 years)). Any status variable related to AT-IR will be based on eCRF. All demographic, Baseline characteristic, UC disease history or characteristics, and prior therapies for UC data will be listed.

11. MEDICAL HISTORY

Medical history data will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). The actual version of the MedDRA coding dictionary will be noted in the statistical tables and Clinical Study Report (CSR).

The number and percentage of subjects in each medical history category (by MedDRA System Organ Class (SOC) and PT) will be summarized overall and by treatment group for the Safety Set.

The SOC and PT within SOC will be presented by descending frequency in the total number of subjects (and alphabetically in the event of a tie).

Subjects reporting more than one condition/diagnosis will be counted only once at each level of summarization (i.e., any, by SOC, or by PT).

All medical history data will be listed. [redacted]

12. PRIOR THERAPIES FOR ULCERATIVE COLITIS (UC)

For subjects with AT-IR (as defined in Section 9.2, based on the PRIOR THERAPIES FOR ULCERATIVE COLITIS eCRF page), the number and percentage of subjects failing each type of medication, overall and by reason for failure (with PT code = '06257601001' (e.g. Stelara, Ustekinumab) re-mapped to medication type = Anti-IL12/23), will be summarized. The following medication types will be excluded from the summary:
- 5-ASA
- Corticosteroid

- Immunosuppressants
- Investigational or New Drug

Subjects will be considered to have failed a medication type if at least one medication of the given type is marked with 'Has the subject failed this therapy?' = Yes. Otherwise, subjects will **not** be considered to have failed the given medication type.

This summary will be repeated for subjects with no AT-IR, including only the following medication types:

- 5-ASA
- Corticosteroid
- Immunosuppressants

Medications with type recorded as "Investigational or New Drug" will be excluded from the summary and listed only.

Additionally, the number and percentage of subjects with AT-IR will be summarized by coded medication name (i.e., preferred name) and by medication type (based on Medication Type, as captured on the PRIOR THERAPIES FOR ULCERATIVE COLITIS eCRF page). Medications with PT code '06257601001' (e.g. Stelara, Ustekinumab) will be re-mapped to medication type = Anti-IL12/23.

A listing of all subjects who were exposed to prior therapies for UC will be provided.

13. PROCEDURES/SURGERIES

All non-drug therapies/procedures within the 30 days prior to first dose of study drug through to the end of study, are captured on the RELATED PROCEDURES/SURGERIES eCRF page. Only this data will be listed.

14. MEDICATIONS

Prior and concomitant medications data (entered on the PRIOR AND CONCOMITANT MEDICATIONS eCRF page) will be coded by the World Health Organization (WHO) Drug Dictionary. The actual version of the WHO Drug Dictionary will be noted in the statistical tables and the CSR. The Safety Set will be used for all presentations of the medications data.

A summary of concomitant medications for UC will be provided by Anatomical Therapeutic Chemical (ATC) Level 4 and preferred name. A similar summary for other concomitant medications will be provided by ATC Level 2 and preferred name. Concomitant medications for UC which started on or after the last dose of study drug by ATC Level 4 and preferred name will also be presented.

Prior medications will include those which started and ended prior to the date of the first dose of study drug; only these will be listed.

Concomitant medications will include those administered between the date of the first dose of study drug and the end of study, inclusive (i.e., all medications starting or ongoing or stopped

during the study). Concomitant medications for UC will be identified via the INDICATION field (equal to UC) on the PRIOR AND CONCOMITANT MEDICATIONS eCRF page. Other concomitant medications will be identified by an INDICATION of AE, Medical History, or Other on the PRIOR AND CONCOMITANT MEDICATIONS eCRF page.

A subject who reports two or more uses of the same medication will be counted only once within each ATC Level and preferred name. A subject reporting more than one medication will be counted only once in the overall total.

Refer to APPENDIX 2 for handling of partial dates for medications. In the case where it is not possible to define a medication as prior or concomitant, the medication will be classified by the worst case (i.e., concomitant).

All medications will be listed.

15. STUDY DRUG EXPOSURE

Study drug exposure will be summarized for each treatment group for the Safety Set. The duration of exposure (days) is defined for each subject as:

Duration of exposure (days) = last dose date–first dose date+1

The last dose date is Date of Treatment Completion/Discontinuation captured on END OF STUDY TREATMENT eCRF page and the first dose date is the earliest Start Date of study drug captured on EXPOSURE eCRF. If the last dose date on the END OF STUDY TREATMENT eCRF and the latest end date on the EXPOSURE eCRF differ (including missing dates), the latest of these dates will be used in deriving study drug exposure and compliance.

Note: Entries on the EXPOSURE eCRF page which are marked with DOSE STATUS = DRUG WITHDRAWAL or DRUG INTERRUPTED will not be considered when deriving the first or last dose date.

Summary statistics will be presented for the duration of exposure (days), as well as the number and percentage of subjects in each of the following treatment duration intervals:

- <2 weeks
- ≥2 weeks–<4 weeks
- ≥4 weeks–<6 weeks
- ≥6 weeks–< 8 weeks
- ≥8 weeks

Interruptions, compliance, and dose changes are not taken into account when calculating the duration of exposure.

Duration on study and total subject years per treatment group will also be displayed. Duration on study is defined for each subject as:

Duration on study (days) = date of study completion/discontinuation–informed consent date+1

Date of study completion/discontinuation is captured on the END OF STUDY eCRF page.

Total subject years is defined for each treatment group as:

Total subject years = sum of the duration on study (days) for all subjects in the treatment group (for the relevant analysis set) divided by 365.25

The number and percentage of subjects who had at least one dose interruption for more than three consecutive days will be displayed. All exposure data, including dose changes, will be listed.

Note: Study drug exposure will be based upon eCRF data only. Daily dosing data collected via the e-Diary will not be presented.

16. STUDY DRUG COMPLIANCE

Compliance is based on the DRUG ACCOUNTABILITY, END OF STUDY TREATMENT, and EXPOSURE eCRF pages and will be calculated as the total number of capsules taken (i.e., the difference between the number of capsules dispensed and the number of capsules returned/lost/damaged) divided by the number of capsules that the subject was expected to take for the length of time that the subject was in the Treatment Phase of the study (i.e., date of last dose–date of first dose+1).

The total number of capsules expected is numerically identical to the subject's duration of exposure, since the medication is to be taken QD.

Overall compliance to study treatment (%) will therefore be calculated as follows:

[(Total no. of capsules dispensed–Total no. of capsules returned–Total no. of capsules lost/damaged)/Study drug exposure in days]*100

Note:

- Blisters **not** returned will be excluded from the compliance calculation for the subject.
- Compliance for subjects discontinuing from the study is determined for the period of their participation in the study up to their last dose date.

Study drug compliance will be summarized for each treatment group for the Safety Set. Summary statistics for overall compliance will be presented as a continuous variable, alongside the number and percentage of subjects with overall compliance in each of the following categories:

- <80%
- ≥80%–≤120%
- >120%

The compliance summary will also include a) the number of treatment kits dispensed, b) the number of treatment kits returned and c) the number of treatment kits **not** returned, per treatment group. Percentages will be displayed for b) and c), where the denominator will be based on the total number of treatment kits dispensed (per treatment group).

Note: b) and c) will be based on the answer to the question "Was the study drug returned?" (a response of 'Yes' implies returned, and a response of 'No' or 'Missing' implies **not** returned).

17. EFFICACY OUTCOMES

All efficacy analyses will be conducted on the FAS.

Unless otherwise specified, any reference to randomization strata used as model factors will be based upon the randomization stratification per IRT. [redacted]

See Section 2.1 for definitions used to assess efficacy outcomes.

17.1. Primary Estimand

17.1.1. Primary Estimand Variables and Derivations

Two separate sets of primary efficacy analyses will be performed to accommodate the varying requirements of the different regulatory agencies. These are each described in turn.

US FDA and national Regulatory Authorities other than EMA Primary Efficacy Endpoint

The primary efficacy endpoint is clinical remission at Week 8.

The SFS, RBS, and MES subscores used to derive Week 8 clinical remission status will be based on the scores/subscores derived in IRT. See APPENDIX 4 for details on how the MMS scores/subscores are derived.

Subjects who achieve clinical remission at Week 8 will be referred to as responders. Subjects who do not achieve clinical remission at Week 8 will be referred to as non-responders. The summary table will include an appropriate footnote to define responders. All subjects with missing clinical remission at Week 8, will be considered as non-responders in the primary analysis with non-responder imputation (NRI).

EU EMA Co-Primary Efficacy Endpoints

Two co-primary efficacy endpoints are endoscopic improvement at Week 8 and symptomatic remission at Week 8.

The SFS, RBS, and MES subscores used to derive Week 8 endoscopic improvement and/or symptomatic remission status will be based upon the subscores derived in IRT.

Subjects who achieve endoscopic improvement/symptomatic remission at Week 8 will be referred to as responders. Subjects who do not achieve endoscopic improvement/symptomatic remission at Week 8 will be referred to as non-responders. The summary table will include an appropriate footnote to define responders. All subjects missing the endpoint at Week 8, will be considered as non-responders in the primary analysis with NRI.

Multiplicity adjustments for these co-primary efficacy endpoints are described in Section 7.5.2.

17.1.2. Intercurrent Event (IE) Handling and Data Imputation for Primary Estimand

Subjects with any of the IEs defined in Section 7.3 occurring prior to Week 8 will be considered to have a known (i.e., non-missing) outcome of non-response in the analysis of all primary efficacy endpoints. Subjects with no IE and a missing efficacy outcome at Week 8 will be included in the primary efficacy analyses as a non-responder.

Analysis visits will be mapped as per Section 6.4 before the above conventions are applied.

17.1.3. Primary Analysis for Primary Estimand

The common risk difference in proportions between the treatment groups in each efficacy endpoint will be estimated using SAS PROC FREQ and Mantel-Haenszel weights adjusting for AT-IR (Yes/No) and Baseline oral corticosteroid usage (Yes/No). Corresponding two-sided 95% and 97.5% CIs and two-sided nominal p-values will be reported for the difference. Point estimate and corresponding two-sided 95% and 97.5% CIs for the OR will also be presented. CIs for the OR will be computed using the Mantel Haenszel method.

Statistical significance will be determined in accordance with the fallback procedure described in Section 7.5. Statistical significance will not be indicated in the TLFs. Instead, the statistical significance of analysis results will be documented and discussed in the CSR.

If there are no responders in a treatment group in any stratum, the difference in percentages and associated inferences can still be made. However, the OR and its CI may be calculated without stratification. This change will be specified in the model footnote present in the output.

US FDA and national Regulatory Authorities other than EMA Primary Efficacy Endpoint

The following statistical hypothesis will be tested:

Obefazimod 50 mg versus placebo:

- [redacted]

Obefazimod 25 mg versus placebo:

- [redacted]

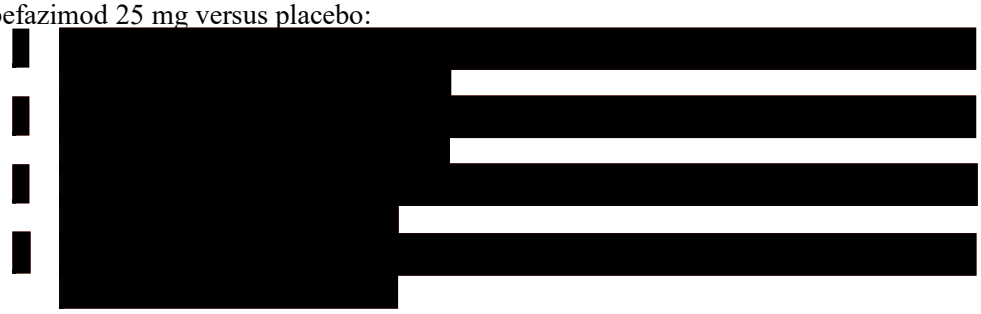
EU EMA Co-Primary Efficacy Endpoints

The following statistical hypotheses will be tested:

Obefazimod 50 mg versus placebo:

- [redacted]

Obefazimod 25 mg versus placebo:



17.1.4. Sensitivity Analysis of Primary Efficacy Variables

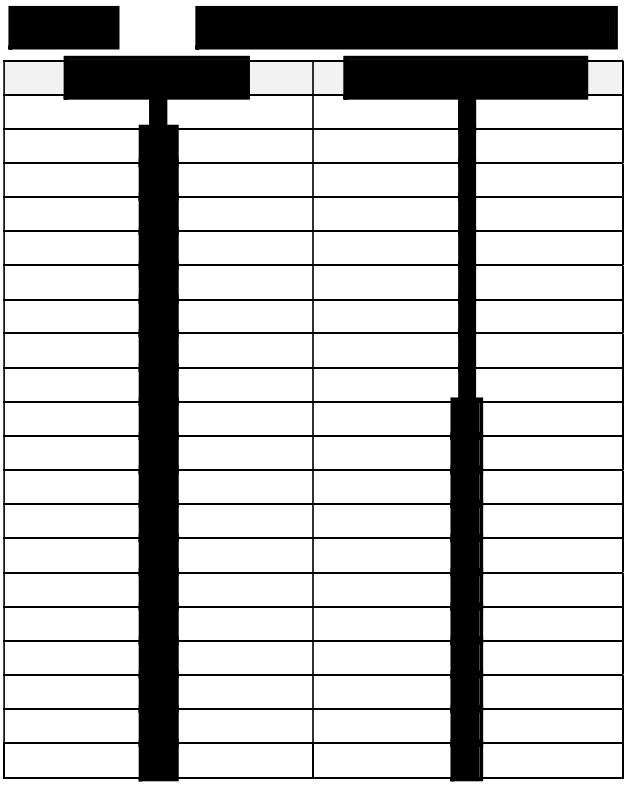
To examine the robustness of the primary efficacy analyses, the following sensitivity analyses will be performed:

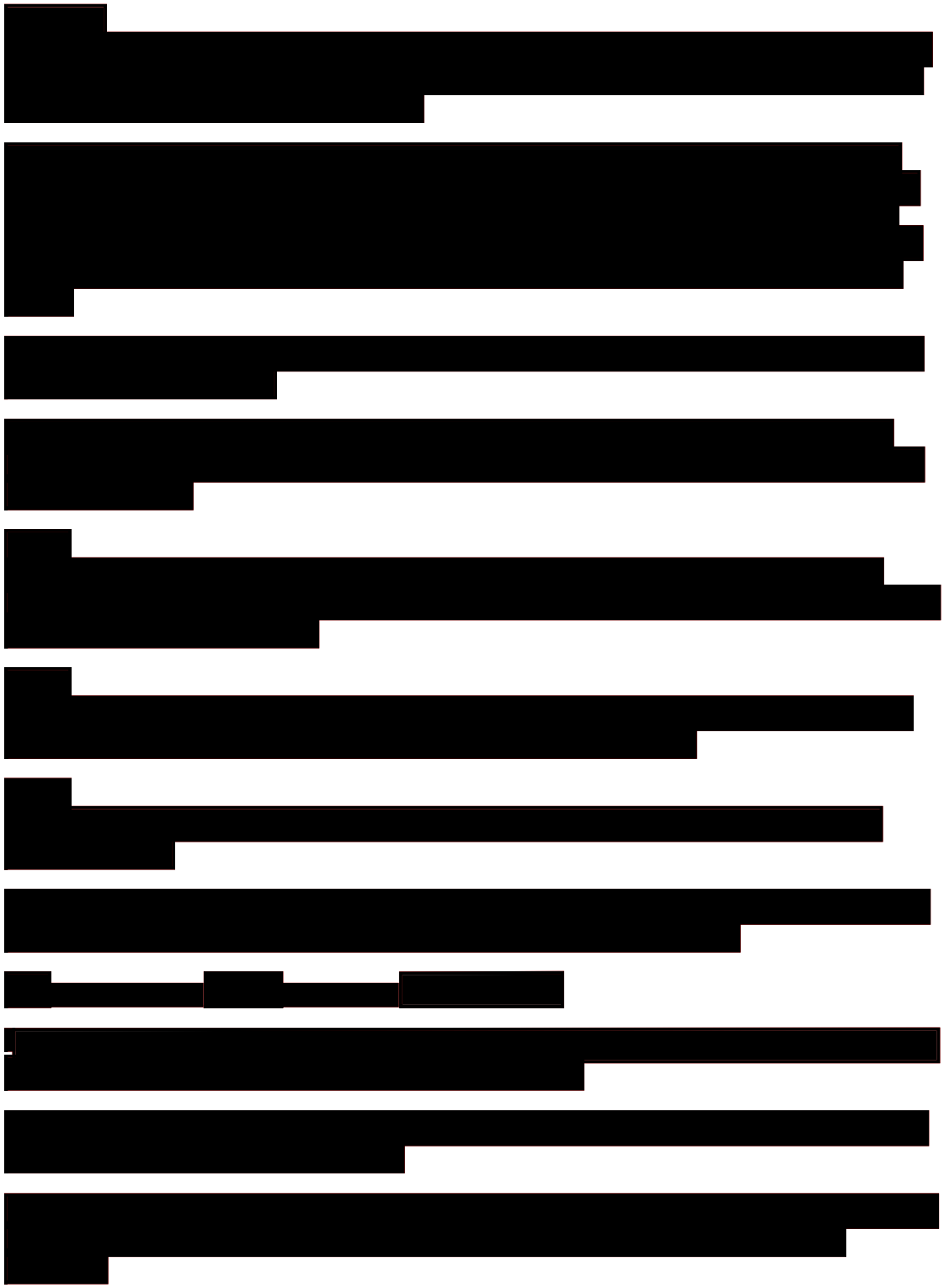
- Sensitivity Analysis #1: Multiple imputation will be used to address missing data; the imputations will be based on outcomes in the placebo group (under a Missing Not at Random (MNAR) assumption)
- Sensitivity Analysis #2: Multiple imputation will be used to address missing data, under the Missing at Random (MAR) assumption.
- Sensitivity Analysis #3: Tipping Point Analysis
- Sensitivity Analysis #4: Recalculation of SFS/RBS/MMS using visit date at Week 8

Each of these sensitivity analyses are described in the following sections.

<u>Sensitivity Analysis #1: Multiple imputation under MNAR assumption</u>

[redacted]





[redacted]

Sensitivity Analysis #2: Multiple imputations (under MAR assumption)

[redacted]

[redacted]

[redacted]

Sensitivity Analysis #3: Tipping Point Analysis

[redacted]

[redacted]

Sensitivity Analysis #4: Recalculation of SFS/RBS/MMS using Visit date at Week 8

[redacted]

17.1.5. Supplementary Analysis of Primary Efficacy Variables

The primary efficacy analyses described in Section 17.1.3 will be repeated using a treatment policy approach (e.g., all types of IE will be ignored). [redacted]

17.1.6. Subgroup Analysis for Primary Efficacy Variables

The consistency of treatment effect for each of the primary efficacy endpoints will be evaluated for the subgroups defined in Section 7.6.

For each of these subgroups, the primary efficacy analysis described in Section 17.1.3 [redacted] nominal level of significance without adjustment for multiplicity. Note that for the subgroups which are confounded with the randomization stratification (Baseline oral corticosteroid use, AT-IR , Number of prior AT-IR by medication name, Number of prior AT-IR by medication type, IR to JAK inhibitors among subjects with AT-IR, and Number of non-JAK inhibitor AT-IR among subjects who have IR to JAK inhibitors), the corresponding stratification variable will be excluded from the model. For example, the subgroup analyses of Baseline oral corticosteroid use will only include the IRT randomization strata of AT-IR in the model. For the other confounding subgroups, the IRT randomization strata of Baseline oral corticosteroid use will be included in the model.

Forest plots will display the results of the overall analysis and each subgroup analysis, for each of the primary efficacy endpoints (i.e., one forest plot for each of the clinical remission at Week 8, endoscopic improvement at Week 8 and symptomatic remission at Week 8 endpoints). These will display the common risk difference in proportions between treatment groups and the corresponding 95% CIs.

17.2. Key Secondary Estimand

17.2.1. Key Secondary Estimand Variables & Derivations

Two separate sets of key secondary efficacy analyses will be performed to accommodate the varying requirements of the different regulatory agencies. These are each described in turn, in each of the following sections.

US FDA and national Regulatory Authorities other than EMA Key Secondary Efficacy Endpoints

The key secondary efficacy endpoints for the US FDA are defined and ordered as:

- Proportion of subjects who achieve endoscopic improvement at Week 8.
- Proportion of subjects with clinical response at Week 8.
- Proportion of subjects with HEMI per Geboes scoring at Week 8.

Endoscopic improvement and clinical response will be determined based on the SFS, RBS, MES and MMS scores/subscores captured in IRT.

HEMI will be determined based on a) the MES and b) the Geboes Index score. The Geboes Index score is derived by subject and visit, in accordance with the details provided in APPENDIX 6.

Multiplicity adjustments for these key secondary endpoints are described in Section 7.5.1.

EU EMA Key Secondary Efficacy Endpoints

The key secondary efficacy endpoints for the EU EMA are defined and ordered as:

- Proportion of subjects who achieve clinical remission at Week 8.
- Proportion of subjects with clinical response at Week 8.
- Proportion of subjects with HEMI per Geboes scoring at Week 8.

Clinical remission and clinical response will be determined based on the SFS, RBS, MES and MMS scores/subscores captured in IRT.

HEMI will be determined based on a) the MES and b) the Geboes Index score. The Geboes Index score is derived by subject and visit, in accordance with the details provided in APPENDIX 6.

Multiplicity adjustments for these key secondary endpoints are described in Section 7.5.2. For all key secondary endpoints (for both US FDA and EU EMA), subjects who achieve the endpoint at Week 8 will be referred to as responders. Subjects who do not achieve the endpoint at Week 8 will be referred to as non-responders. Tables will include appropriate footnotes to define responders. All subjects with missing endpoint at Week 8, will be considered as non-responders.

17.2.2. Intercurrent Event (IE) Handling and Data Imputation for Key Secondary Estimand

IE handling and missing data imputation for the key secondary efficacy variables will mirror the approach used for the primary efficacy endpoints, as described in Section 17.1.2.

17.2.3. Primary Analysis for Key Secondary Efficacy Estimand

The key secondary endpoints will each be analyzed using the same statistical approach as that used for the primary endpoint (per details in Section 17.1.3) with analogous hypotheses (i.e., the null hypothesis is no difference between obefazimod 50 mg and placebo, and no difference between obefazimod 25 mg and placebo).

Achievement of statistical significance in key secondary efficacy endpoints will only be claimed if statistical significance is achieved for the primary analysis of the corresponding primary efficacy endpoint(s). The statistical significance of each key secondary efficacy endpoint comparison will be determined in accordance with the fallback procedure described in Section 7.5. Statistical significance will not be indicated in the TLFs. Instead, the statistical significance of analysis results will be documented and discussed in the CSR.

US FDA and national Regulatory Authorities other than EMA Key Secondary Efficacy Endpoints

Key secondary efficacy endpoints will be compared in the order described in Section 17.2.1. The comparisons will be conducted in accordance with the details of the fallback procedure described in Section 7.5.1.

EMA Key Secondary Efficacy Endpoints

Key secondary efficacy endpoints will be compared in the order described in Section 17.2.1. The comparisons will be conducted in accordance with the details of the fallback procedure described in Section 7.5.2.

17.2.4. Sensitivity Analysis for Key Secondary Efficacy Variables

All sensitivity analyses will be conducted for each set of key secondary efficacy endpoints (i.e., US FDA and national Regulatory Authorities other than EMA), mirroring the approach described for the primary efficacy endpoints in Section 17.1.4.

17.2.5. Supplementary Analysis for Key Secondary Efficacy Variables

The supplementary analysis described for the primary efficacy endpoints in Section 17.1.5 will be repeated for each set of key secondary efficacy endpoints (i.e., US FDA and national Regulatory Authorities other than EMA).

17.2.6. Subgroup Analysis for Key Secondary Efficacy Variables

The consistency of treatment effect for each of the key secondary efficacy endpoints will be evaluated for the subgroups defined in Section 7.6.

For each of these subgroups, the primary efficacy analysis described in Section 17.1.3 will be repeated at 5% (two-sided) nominal level of significance without adjustment for multiplicity. Note that for those subgroups which are confounded with the randomization stratification (where all subjects in a subgroup have the same randomization stratification), it will not be possible to adjust for that randomization stratification within the analysis.

Forest plots will display the results of the overall analysis and each subgroup analysis, for each of the key secondary efficacy endpoints (i.e., one forest plot for each key secondary endpoint). These will display the common risk difference in proportions between treatment groups and the corresponding 95% CIs.

17.3. Other Secondary Efficacy Endpoints

All other secondary efficacy endpoints will be tested in an exploratory setting.

17.3.1. Other Secondary Efficacy Variables & Derivations

Other secondary endpoints include the following categorical endpoints:

- Proportion of subjects in partial clinical response by visit (i.e., Week 4 and Week 8)
- Proportion of subjects with symptomatic remission by visit (i.e., Week 4 and Week 8)
- Proportion of subjects with an RBS=0 by visit (i.e., Week 4 and Week 8)
- Proportion of subjects with ≥1 point RBS improvement from Baseline by visit (i.e., Week 4 and Week 8)
- Proportion of subjects with an SFS=0 or 1 by visit (i.e., Week 4 and Week 8)
- Proportion of subjects with ≥1 point SFS improvement from Baseline by visit (i.e., Week 4 and Week 8)
- Proportion of subjects with BU=0 by visit (i.e., Week 4 and Week 8) in the subpopulation of subjects with BU at Baseline
- Proportion of subjects with FC below 150 µg/g by visit (i.e., Week 4 and Week 8)
- Proportion of subjects with histologic improvement per Geboes scoring at Week 8
- Proportion of subjects with endoscopic remission at Week 8
- Proportion of subjects with HEMR per Geboes scoring at Week 8
- Proportion of subjects with histologic remission per Geboes scoring at Week 8
- Proportion of subjects with IBDQ response at Week 8
- Proportion of subjects with no NBM by visit (i.e., Week 4 and Week 8), in the subpopulation of subjects with NBM at Baseline
- Proportion of subjects with no EIM at Week 8, in the subpopulation of subjects with EIM at the Baseline visit
- Proportion of subjects with UC related health care encounters

Other secondary endpoints also include the following continuous endpoints:

- Change from Baseline in MMS at Week 8
- Change from Baseline in pMMS by visit (i.e., Week 4 and Week 8)
- Change from Baseline in RBS by visit (i.e., Week 4 and Week 8)
- Change from Baseline in SFS by visit (i.e., Week 4 and Week 8)
- Change from Baseline in FC (log-transformed for analysis) by visit (Week 4 and Week 8)
- Change from Baseline in Fatigue NRS by visit (Week 4 and Week 8)
- Change from Baseline in FACIT-Fatigue score at Week 8
- Change from Baseline in IBDQ total score and IBDQ dimension scores at Week 8
- Change from Baseline in EQ-5D-5L index score by visit (Week 4 and Week 8)
- Change from Baseline in hsCRP by visit (Week 4 and Week 8)
- Change from Baseline in WPAI:UC scores at Week 8
- Change from Baseline in miR-124 expression in rectal/sigmoidal biopsies at Week 8

- Change from Baseline in miR-124 expression in total blood by visit (i.e., Week 4 and Week 8)

Change from Baseline in Cytokine plasma concentrations by visit (Week 4 and Week 8) overall, and in subgroups (clinical remission and clinical responders) MMS will be considered missing if any component subscore of MMS is missing.

The details of any derivations required to calculate the above endpoints are described below. Endpoints involving MMS, pMMS, RBS, SFS or MES will be based on scores/subscores derived in IRT.

Geboes Scoring
Geboes Index score will be derived in accordance with the details provided in APPENDIX 6, and used to derive the histology related endpoints.

Extraintestinal Manifestations (EIM)
Subjects will be considered to have no EIM at a given visit (Baseline visit or Week 8 visit) if the EIM eCRF page was marked to indicate that an EIM review was performed at that visit, and all individual EIMs were marked as 'No.'

UC-related Health Care Encounters
Subjects will be considered to have had a UC-related health care encounter if they have at least one encounter documented on the HEALTH CARE ENCOUNTERS eCRF page, with start date after date of first dose of study drug.

Bowel Urgency (BU)
BU is reported by the subject daily (yes or no), in an e-Diary, using a 24-hour recall period. eDiaries are issued at the Screening visit and completed daily through to Week 8 or end of treatment.

Nocturnal Bowel Movements (NBM)
NBM (one or more sleep interruptions due to bowel movement) is reported by the subject daily in the e-Diary (Yes/No) using a 24-hour recall period.

[redacted]

Inflammatory Bowel Disease Questionnaire (IBDQ) Scores
IBDQ scores (total and per dimension) are derived by visit, in accordance with the details provided in APPENDIX 7.

European Quality of Life 5 Dimensions 5 Level (EQ-5D-5L) Questionnaire
EQ-5D-5L scores are derived by visit, in accordance with the details provided in APPENDIX 8.

Fatigue Numeric Rating Scale (NRS)
Fatigue NRS values are derived by visit, in accordance with the details provided in APPENDIX 9.

Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue
The FACIT-Fatigue subscale score is derived by visit, in accordance with the details provided in APPENDIX 10.

Work Productivity and Activity Impairment Questionnaire: Ulcerative Colitis (WPAI:UC)
WPAI:UC scores are derived by visit, in accordance with the details provided in APPENDIX 11.

17.3.2. Missing Data and Data Imputation for Other Secondary Efficacy Variables

For all categorical other secondary efficacy endpoints (except UC-related health care encounters), unless otherwise stated, subjects with any of the IEs defined in Section 7.3 that occur prior to the visit of interest (i.e., Week 4 or Week 8) will be considered to have a known (i.e., non-missing) outcome of non-response. [redacted] one UC-related healthcare encounter, with a start date after first dose of study drug.

For continuous other secondary efficacy endpoints, assessments which occurred after any of the IEs defined in Section 7.3 will be excluded (i.e., considered missing).

Missing continuous outcome data will not be imputed for the ANCOVA analysis. However, they will be handled by implicit imputation in the MMRM analysis, with missingness assumed as MAR. Further details of these analyses are provided in Section 17.3.3.

17.3.3. Analysis of Other Secondary Efficacy Variables

Categorical Endpoints

The categorical endpoints outlined in Section 17.3.1 will each be analyzed using the same statistical approach as that used for the primary endpoint (per details in Section 17.1.3). Note however, that the fallback procedure (described in Section 7.5) does not apply to

these endpoints and hence only 95% CIs will be calculated/displayed.

Continuous Endpoints

Aside from the analysis of miR-124 endpoints (which is described below), the continuous endpoints which were scheduled to be assessed only at a single post-Baseline timepoint (e.g., change from Baseline in MMS at Week 8) outlined in Section 17.3.1 will be analyzed using an ANCOVA for the change from Baseline, including treatment and the randomization stratification variables as fixed factors, and the Baseline level of the outcome of interest as a covariate.

Continuous endpoints which were scheduled to be assessed at multiple post-Baseline timepoints (e.g., change from Baseline in RBS at Week 4 and Week 8) outlined in Section 17.3.1 will be analyzed using an MMRM. This model will include fixed categorical effects for treatment, visit, treatment-by-visit interaction and randomization stratification factors, as well as fixed continuous effects for the Baseline value of the outcome of interest. An unstructured covariance matrix will be used to model the within-subject variance-covariance structure. If the unstructured covariance matrix fails to converge, the following methods will be applied (in this order, until convergence is achieved): heterogeneous Toeplitz, heterogenous compound symmetry.

Both the ANCOVA and MMRM analysis results will be presented using the least square mean by treatment group and difference between each obefazimod dose group and placebo for each applicable post-Baseline timepoint, together with the corresponding two-sided 95% CIs and two-sided p-value. For the MMRM analysis of log-transformed change from Baseline in FC, the least square mean difference will be back-transformed (exponentiated) and presented as the LS mean percentage difference (obefazimod versus placebo), by subtracting 1 and multiplying by 100%.

Subjects with no Week 8 measurement per the windowing conventions described in Section 6.4 will be excluded from the ANCOVA for the corresponding endpoint. Subjects with no Week 4 **and** no Week 8 measurement will be excluded from the MMRM analysis of the corresponding endpoint.

Values and change from Baseline in continuous outcome measures will also be summarized by visit via summary statistics. For FC, the percent change from Baseline values will also be included in the summary.

The mean change from Baseline will also be plotted, by treatment group and visit for FC and hsCRP.

Note that cytokine plasma concentrations which are below the lower limit of quantification (LLQ), or above the Upper Limit of Quantification (ULQ), will be converted to the LLQ (or ULQ) value, for the purpose of quantitative summaries and analyses, but will be presented, as recorded, in the listings.

Analysis of miR-124

[redacted]

17.4. Exploratory Efficacy Endpoints

In addition to the by-visit PRO endpoints specified in Section 17.3.1, the following daily diary items will be summarized by Week (i.e., for Week 1 (Days 1-7) through to Week 8 (Days 50-56)), via summary statistics.

- SF
- RB
- pMMS
- NBM
- BU
- Fatigue NRS

Weekly SF, RB and pMMS values will also be plotted, by treatment group.

Weekly SF, RB and Fatigue NRS scores will be defined as the mean of the daily scores entered into the e-Diary for the 7 days leading up to the timepoint (e.g., Week 5 score comprises the mean of the daily diary entries made on Days 29-35), rounded to the nearest integer. For any weeks that fall within an endoscopy assessment, the day of bowel prep and day of endoscopy will be excluded from the weekly SF/RB subscore derivations. Weekly scores will only be derived if daily entries are available for at least three days in the 7 days leading up to the timepoint.

Note: The weekly SF and RB at the 4th week and the 8th week may not match the Week 4 and Week 8 RBS/SFS respectively, due to difference in the derivation method and windowing convention.

Weekly pMMS scores will be defined as the sum of the corresponding weekly SF and RB scores.

Weekly BU and NBM scores will be defined as the total number of days on which the subject experienced the symptom, over the 7 days leading up to the timepoint. For any weeks that fall within an endoscopy assessment, the day of bowel prep and day of endoscopy will be excluded from the weekly score derivation. If there are missing assessments but at least 3 days with data in the 7 days leading up to the timepoint, the BU/NBM scores will be averaged then multiplied by 7 to get an average weekly score (e.g., if 4 of 7 days have data, BU/NBM score will be sum of the 4 days/4*7), rounded to the nearest integer.

In the event a subject reports multiple scores for a parameter on the same day, which can happen if a) the subject starts the assessment close to midnight, but completes/submits it after midnight, and completes another assessment later that day or b) the subject utilizes more than one device for the assessment, the assessment with the latest response time on that day is considered for the above derivations.

The relevant Study Days for each of the Weekly endpoint derivations are provided in Table E below. Note that Baseline is included here (derived analogously to the weekly scores described above), because this will feature in the MMRM analysis of the weekly scores (further details provided below).

Table E: Study Days Used for Weekly Endpoint Derivations

Timepoint	Study Days
Baseline	-7 to -1 (or -6 to 1)* (i.e. 7 days prior to first dose)
Week 1	1 to 7
Week 2	8 to 14
Week 3	15 to 21
Week 4	22 to 28
Week 5	29 to 35
Week 6	36 to 42
Week 7	43 to 49
Week 8	50 to 56

** Assessments on Day 1 will only be used for Baseline if they are recorded prior to the start of study treatment.*

Each of the weekly endpoints will be analyzed using an MMRM. This model will include fixed categorical effects for treatment, week, treatment-by-week interaction and randomization stratification factors, as well as fixed continuous effects for the Baseline value of the outcome of interest. An unstructured covariance matrix will be used to model the within-subject variance-covariance structure. If the unstructured covariance matrix fails to converge, the following methods will be applied (in this order, until convergence is achieved): heterogeneous Toeplitz, heterogenous compound symmetry.

The MMRM analysis results will be presented using the least square mean by treatment group and difference between each obefazimod dose group and placebo for each week (Week 1 to Week 8), together with the corresponding two-sided 95% CIs and two-sided p-value. Consistent with the analysis of continuous other secondary efficacy variables, weekly endpoint assessments which occurred after any of the IEs defined in Section 7.3 will be considered missing.

Additionally, the number and percentage of subjects with Fatigue remission at Week 8 and the number and percentage of subjects with IBDQ remission at Week 8 will be analyzed and summarized analogously to the categorical other secondary efficacy endpoints, as described in Section 17.3.

Note: Only subjects with assessments below the criteria for Fatigue remission or IBDQ remission at Baseline will be included in the Week 8 analyses.

The number and percentage of subjects with FC below 150 µg/g and with FC below 250 µg/g will also be summarized, by visit.

18. SAFETY OUTCOMES

All outputs for safety outcomes will be based on the Safety Set except outputs for cardiac sub-study outcomes will be based on the Cardiac Function Set.

18.1. Adverse Events (AEs)

AEs will be coded using the standard dictionary (MedDRA) down to the lower-level term. The actual version of the MedDRA coding dictionary will be noted in the statistical tables and CSR.

The severity of AEs will be assessed by the investigator, according to Common Terminology Criteria for Adverse Events (CTCAE) Classification Version 5.0 (grade 1=mild, grade 2=moderate, grade 3=severe, grade 4=life-threatening and grade 5=fatal).

18.1.1. Treatment-Emergent Adverse Events (TEAEs)

TEAEs are defined as any AE which started or worsened in severity from a pre-existing AE after the first dose of study drug. The algorithm for determining treatment emergence for events with partial or missing onset and/or end dates, is described in APPENDIX 2.

In the case where it is not possible to define an AE as treatment-emergent or not, the AE will be classified as treatment-emergent.

In general, AEs which start on the date of first dose of study drug, will be considered treatment-emergent, except for AEs which are considered 'laboratory-related' (see APPENDIX 12) and pertain to laboratory samples which were drawn prior to the time of administration of first dose of study drug. For laboratory-related AEs, the time of first dose of study drug will be compared to the laboratory sample time to ascertain treatment-emergent status. If there are multiple lab sample times on this date (e.g., stool sample time and serum sample time) then the earliest of these laboratory sample times will be used. If the laboratory sample time is missing, or if the time of first dose is missing, the laboratory-related AE will be considered treatment-emergent.

An overall summary table will be presented, which will include the number and percentage of subjects and number of events for each of the following types:

- any AE
- any TEAE
- any TEAE related to study drug
- any TEAE leading to study drug interruption
- any related TEAE leading to study drug interruption
- any TEAE leading to study drug discontinuation
- any related TEAE leading to study drug discontinuation
- any serious TEAE
- any related serious TEAE
- any TEAE leading to death
- any TEAE by maximum CTCAE grade (Grade 1, Grade 2, Grade 3, Grade ≥4)

- any treatment-emergent AESI

For the purpose of summary tabulations, a related TEAE is considered any TEAE with relationship to study treatment marked as Related, Probably Related or Possibly Related. Events with a missing relationship will be considered related. Every effort will be made to ensure that there are no events with missing relationship. No events with missing severity or seriousness are expected.

Separate tabular summaries will be presented by MedDRA SOC and PT for each of the following:

- TEAEs
- TEAEs by maximum CTCAE grade
- TEAEs by maximum relationship
- Related TEAEs
- Related TEAEs by maximum CTCAE grade
- Serious TEAEs
- Serious TEAEs by maximum CTCAE grade
- Serious TEAEs by maximum relationship
- Related Serious TEAEs by maximum CTCAE grade
- Non-serious TEAEs
- TEAEs leading to study drug interruption
- TEAEs leading to study drug discontinuation
- TEAEs leading to study discontinuation
- TEAEs of grade ≥3

These summaries will be sorted by decreasing order of total subject frequency in the obefazimod 50 mg group per SOC and PT, and by alphabetical order when these frequencies are tied. Subjects will be reported once at each level of summarization.

All AEs will be listed. Additionally, listings for deaths during the study, serious TEAEs, AEs leading to study drug discontinuation, and AESIs will be presented.

18.1.2. Treatment-Emergent Adverse Events (TEAEs) per Subject-Years of Exposure

In addition to the summaries described above, TEAE incidence rates per 100 subject-years of exposure will be provided for each TEAE category in the AE overview summary and for all TEAEs by SOC and PT.

- **Total Exposure (years)** is defined per subject as either a) time (days) from first dose to the onset of first event for those who experienced the AE, or b) time (days) from first dose to end of study for those who did not experience the AE. This is summed across all subjects in the treatment group and normalized by 365.25. Total exposure is displayed to one decimal place in the summaries, though unrounded values are used to derive incidence rates.
- **Incidence Rate** is defined as the number of subjects with the AE, divided by total exposure. Incidence rate is reported per 100 subject years, per treatment group.

Incidence rates will be compared (each obefazimod dose group versus placebo) for each

of the following event types in turn. Unadjusted risk differences will be presented, along with corresponding two-sided 95% CIs, using the Wilson's score method:

- Serious TEAEs
- TEAEs leading to study drug discontinuation
- Treatment-emergent AESIs
- Treatment-emergent skin lesions AESI
- Treatment-emergent headaches AESI
- Treatment-emergent anemia AESI
- Treatment-emergent hepatic enzyme elevations AESI
- Treatment-emergent serious or severe (grade ≥3) infections AESI
- Treatment-emergent opportunistic infections AESI
- Treatment-emergent acute pancreatitis AESI
- Treatment-emergent malignancies including non-melanoma skin cancers AESI
- Treatment-emergent cardiac abnormalities suggestive of cardiac fibrosis AESI

18.1.3. Adverse Events of Special Interest (AESIs)

AESIs are defined in the Clinical Study Protocol Section 8.1.2. All AESIs indicated on the ADVERSE EVENTS eCRF page will be reviewed prior to database lock. [redacted] AESIs will be classified in the following categories and sub-categories:

- [redacted]
- Headaches
- Anemia
- Hepatic enzyme elevations
- Serious or severe (grade ≥3) infections and opportunistic infections

[redacted]

A Custom MedDRA Query (CMQ) search strategy will map PTs to each AESI category and subcategory based on a blinded data review.

For the [redacted] category, narrow search terms have been assigned to Category A and the broad search terms have been assigned to Category B (laboratory terms) and Category C (signs and symptom terms). AEs in Category A will be mapped to the [redacted] AESI category. AEs in Categories B and C need to exist together and be temporally associated (start dates for these events must be within +/-7 days of each other) in order to be mapped to the [redacted] AESI category. If the AE start dates are partial, they will be considered temporally associated unless the partial start date information clearly rules that out.

For the serious and severe infection category, in addition to the PT being in the CMQ list, either seriousness needs to be 'Yes' or grade needs to be 'Grade 3' or higher for the AE to be mapped to the AESI category.

AESIs will be presented by category, sub-category and PT. Subjects will only be counted once per category, sub-category and PT. Some PTs fall under multiple categories (and subcategories), in which the subject will be counted in each category (and subcategory) and PT but at most once at each summarization level.

Note: For the [redacted] AESI category, laboratory PTs and all temporally associated sign and symptom PTs will be concatenated and displayed. For example, if [redacted] on Day 10, [redacted] occurred on Day 15 and [redacted] increased on Day 20, there will be two PT terms in the analyses, displayed as [redacted] on Day 10, [redacted] occurred on Day 12 and [redacted] on Day 14, there will be three PT terms in the analyses, displayed as [redacted]

An additional summary of treatment-emergent headaches will be presented. Specifically, the number and percentage of subjects who experienced any treatment-emergent headache, will be presented, as well as the total number of treatment-emergent headache events. Headaches will be identified using the CMQ search strategy for the Headache category. The tabular summary will also include:

- Duration of headache (days) for the longest treatment-emergent headache per subject
- Time to onset of first treatment-emergent headache per subject (days)
- Duration of headache (days) for all treatment-emergent headaches
- Treatment-emergent headache outcome (per event)
- Treatment given – Yes/No (per event)
- Action taken with study drug (per event)
- AESI – Yes/No (per event)
- Headache led to study discontinuation (per subject)

For the percentage summary per subject, the denominator will be the number of subjects in the analysis set. For the percentage summary per event, the denominator will be the number of all events. This summary will be repeated for treatment-emergent AESI headaches as well.

18.2. Deaths

If any subjects die during the study (recorded on the DEATH DETAILS eCRF page), the information will be presented in a data listing.

18.3. Laboratory Evaluations

The analysis of laboratory data will be based on central laboratory assessments only. Any local laboratory test results are kept with the subject's source data, but not captured on the eCRF – only the clinical significance and any associated AEs are reported for local laboratory test results.

The clinical laboratory parameters assessed at central laboratories are defined in the Clinical Study Protocol Table 4.

In general, presentations will use SI units. Quantitative laboratory measurements reported as '<X' or '>X', where X may be the LLQ or the ULQ, respectively, will be converted to

X for the purpose of quantitative summaries, but will be presented as recorded (i.e., '<X' or '>X') in the listings.

Only laboratory tests with non-missing results from at least 50 randomized subjects will be summarized in tables.

18.3.1. Hematology and Biochemistry

Hematology and biochemistry test results will be summarized per parameter and visit via summary statistics. The change from Baseline to each applicable post-Baseline visit will also be summarized. End of treatment values will be included in this summary.

A shift table from Baseline to worst post-Baseline value (categorized as low, normal or high, based on the laboratory normal range) will be created for hemoglobin (HGB), alanine transaminase (ALT), aspartate aminotransaminase (AST), total bilirubin (TBL), [redacted] For HGB, the lowest assessment will be considered the worst. For the other parameters, the highest assessment will be considered the worst. When selecting the worst post-Baseline assessments, only on-treatment results will be considered.

A similar shift table will be provided to summarize shifts from Baseline to end of treatment for all parameters.

All hematology and biochemistry results will be listed. Values outside of the laboratory normal range will be flagged.

A summary table for [redacted] (>3*Upper Limit of Normal (ULN)) and [redacted] (>3*ULN) assessments will be presented by visit. End of treatment and maximum post-Baseline values will also be included in this summary. Additionally, a listing of all [redacted] assessments over time when at least one assessment is elevated (>3*ULN) will be provided.

18.3.2. Assessment of Liver Enzyme Elevations

Liver-specific laboratory tests include ALT, AST, alkaline phosphatase (ALP), and TBL. The number and percentages of subjects with liver specific function test values that meet the following criteria of potential clinical interest will be summarized by treatment group and visit:

- ALT >3, 5, 8, 10, 20*ULN
- AST >3, 5, 8, 10, 20*ULN
- TBL ≥2*ULN
- ALP ≥1.5*ULN
- ALT and/or AST >3*ULN and TBL ≥1.5*ULN
- ALT and/or AST >3*ULN and (TBL >2*ULN or International Normalized Ratio (INR) >1.5)
- ALT and/or AST >3*ULN with appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia >5%

End of treatment and maximum post-Baseline value will also be included in this summary.

For the by visit summary, for criteria that involve multiple parameters (i.e., ALT/AST,

TBL, INR), if the ALT and/or AST analysis visit value meet the specified condition (i.e., >3*ULN), then the TBL/INR values **from the same sample date** will be evaluated for the other parts of the criterion (regardless of whether the TBL/INR are flagged as the same analysis visit value). Subjects will be counted in the denominator for the visit if they have non-missing values for all parameters included in the criterion, based on this selection method.

For the maximum post-Baseline summary, the maximum post-Baseline ALT and AST value per subject will be selected (if the maximum value, per parameter, occurs on more than one occasion, that with the highest associated TBIL value will be selected). This will be assessed relative to the criterion, based on other parameter values (TBIL, INR) **that pertain to the same sample date**. Subjects will be counted in the denominator if they have non-missing values for all parameters included in the criterion, based on this selection method. If a value satisfies more than one criteria per parameter (i.e., >3*ULN and >5*ULN) then the subject will be counted once, in the highest criteria satisfied. Subjects can be counted more than once in different laboratory criteria (i.e. ALT >3*ULN and ALP ≥1.5*ULN).

Subjects are considered to have met the last criterion listed above (i.e., ALT and/or AST >3*ULN with appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia >5%) if an AE with any one of the below PTs occurs within 7 days of the elevated ALT and/or AST value:

- Fatigue
- Nausea
- Vomiting
- Abdominal pain, Abdominal pain upper, Abdominal tenderness, Liver tenderness
- Pyrexia
- Rash, Rash macular, Rash papular, Rash maculo-papular, Rash pruritic
- Eosinophilia, Eosinophil count increased, Eosinophil count abnormal, Eosinophil percentage increased, Eosinophil percentage abnormal

A listing of potentially clinically significant liver function laboratory values will be provided. The listing will include all ALT, AST, ALP and TBL results for subjects who met any of the following 4 criteria:

- ALT >3*ULN,
- AST >3*ULN,
- ALP ≥1.5*ULN, or
- TBL ≥1.5*ULN

In addition, eDISH plots will be created displaying the following:

- Maximum AST versus same-day TBL
- Maximum ALT versus same-day TBL

Only post-Baseline concentration values will be considered. The maximum value for each subject and each parameter (AST or ALT) will be calculated independent of visit designation. If the maximum AST/ALT assessment occurs at 2 different dates, the assessment with the higher accompanying bilirubin value will be used. The below regions will be marked on each eDISH plot:

- AST or ALT >3*ULN and TBL >2*ULN = Hy's Law range

- AST or ALT <3*ULN and TBL >2*ULN = Gilbert's Cholestasis range
- AST or ALT >3*ULN and TBL <2*ULN = Temple's Corollary range
- AST or ALT <3*ULN and TBL <2*ULN

18.3.3. [redacted]

[redacted]

18.3.4. Serology

Serology assessments are due at Screening only. Results will be listed.

18.3.5. Microbiology

Microbiology assessments are due at Screening only. Results will be listed.

18.4. Pregnancy Test Results

Female subjects of childbearing potential are required to be tested for pregnancy via urine beta-human chorionic gonadotropin (β-hCG) and/or serum β-hCG pregnancy tests throughout the study. All pregnancy test results will be listed for subjects who have at least one positive result.

18.5. Vital Signs

Vital signs assessments include weight (kg), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), heart rate (bpm) and body temperature (˚C). The investigator will additionally classify each of blood pressure, heart rate and temperature as either Normal, Abnormal not clinically significant (Abnormal NCS), or Abnormal clinically significant (Abnormal CS).

Quantitative vital signs results will be summarized per parameter and visit via summary statistics. The change from Baseline to each applicable post-Baseline visit will also be summarized. End of treatment will be included in this summary. The mean change from Baseline will also be plotted, by treatment group and visit for systolic blood pressure,

diastolic blood pressure, and heart rate.

The incidence of markedly abnormal values (as defined in Section 18.5.1) will be displayed by visit and at end of treatment.

In addition, a shift table for the change in investigator assessment (Normal, Abnormal NCS and Abnormal CS) from Baseline to end of treatment will be displayed for blood pressure, heart rate and temperature.

All vital signs results will be listed with abnormal values flagged. A listing of all vital signs results for subjects meeting any markedly abnormal criteria at least once will also be provided.

18.5.1. Vital Signs Markedly Abnormal Criteria

Markedly abnormal quantitative vital signs measurements will be identified in accordance with the following predefined markedly abnormal criteria (Table F).

Table F: Markedly Abnormal Criteria for Vital Signs

Variable	Unit	Low	High
Systolic blood pressure	mmHg	≤90 **and** change from Baseline ≤-20	≥180 **and** change from Baseline ≥20
Diastolic blood pressure	mmHg	≤50 **and** change from Baseline ≤-15	≥105 **and** change from Baseline ≥15
Heart rate	bpm	≤50 **and** change from Baseline ≤-15	≥120 **and** change from Baseline ≥15
Body temperature	˚C	N/A	≥38.3 **and** change from Baseline ≥1.1
Weight	kg	percentage change from Baseline ≤-5.0 %	percentage change from Baseline ≥5.0 %

18.6. ECG Evaluations

ECGs are performed locally. The following ECG parameters are reported for this study:

- PR Interval (msec)
- QRS Interval (msec)
- QT Interval (msec)
- QTc Interval (msec) (either Bazett or Fridericia correction)
- ECG interpretation (normal or abnormal)
- ECG finding (for abnormal results)
- Clinically significant (Yes/No)

Values and changes from Baseline in quantitative ECG results will be summarized by descriptive statistics, by treatment group and visit, and at end of treatment.

QT intervals with Bazett correction (QTcB) will be converted to QT interval with Fridericia correction (QTcF) prior to summarization. This conversion will be performed via the following steps:

- Firstly, derive RR = $(QT/QTcB)^2$
- Next, derive QTcF = $QT/\sqrt[3]{(RR)}$

The incidence of markedly abnormal values (as defined in Section 18.6.1) will be displayed by visit and at end of treatment, as well as a shift table for the change in markedly abnormal categories on absolute values only from a) Baseline to end of treatment and b) Baseline to worst post-Baseline assessment.

All ECG results will be listed with markedly abnormal values flagged. A listing of all ECG assessments in subjects meeting any markedly abnormal criteria at least once will also be provided.

18.6.1. ECG Markedly Abnormal Criteria

Markedly abnormal quantitative ECG measurements will be identified in accordance with the following predefined markedly abnormal criteria:

- Absolute values for QTcF will be classified as:
  - >450 msec for males or >460 for females
  - >480 msec
  - >500 msec
- Change from Baseline QTcF will be classified as:
  - >30 msec increase from Baseline
  - >60 msec increase from Baseline

In shift tables, subjects will be classified as markedly abnormal if any of the above criteria for absolute QTcF values are met.

18.7. Physical Examination

Physical examinations are performed at each visit, and include the eyes, ears, nose, throat, lungs/thorax, heart/cardiovascular system, abdomen, skin and mucosae, nervous system, lymph nodes, musculoskeletal system, and, if applicable, other parts of the body. If there are any new or worsening clinically significant abnormalities, these are captured as either Medical History or AEs. No other physical examination outcome data is captured, and hence there will be no stand-alone physical examination summaries or listings.

18.8. [redacted]

19. PHARMACOKINETICS (PK)

The obefazimod and concentration data mapping (Study Data Tabulation Model) will be produced by . The descriptive summary analysis of concentration data and the inclusion of data in an integrated population PK analysis (described in Section 9.6 of the Clinical Study Protocol) will be addressed in a separate PK SAP and population modelling analysis plan for population PK, respectively, both produced by

20. REFERENCES

Guyatt G, Mitchell A, Irvine E J, Singer J, Williams N, Goodacre R, Tompkins C. "A new measure of health status for clinical trials in inflammatory bowel disease." *Gastronenterology* (1989): 96: 804-10.

Pickard S, Law E, Jiang R, Pullenayegum E, Shaw J, Xie F, Oppe F, Boye K, et al. "United States Valuation of EQ-5D-5L Health States Using an International Protocol." *Value Health* (2019): 22(8):931–941.

Ratitch B., Lipkovich I., O'Kelly M. "Combining Analysis Results from Multiply Imputed Categorical Data." *PharmaSUG* (2013): Paper SP03.

Rubin, D.B. "Multiple imputation for nonresponse in surveys." *New York: John Wiley and Sons* (1987).

U.S. Food and Drug Administration. "Guidance for industry: Ulcerative Colitis: Developing Drugs for Treatment." *U.S. Department of Health and Human Services Food and Drug Administration* (2022)

APPENDIX 1. NQUERY SAMPLE SIZE CALCULATIONS

Sample Size Calculation 1

Clinical remission, obefazimod 50 mg versus placebo, type I [redacted] (two-sided):

[redacted]

Sample Size Calculation 2

Clinical remission, obefazimod 25 mg versus placebo, type I [redacted] (two-sided):

[redacted]

Sample Size Calculation 3

Clinical remission, obefazimod 50 mg versus placebo, difference [redacted] subjects [redacted], type I [redacted] (two-sided):

[redacted]

Sample Size Calculation 4

Clinical remission, obefazimod 50 mg versus placebo, difference [redacted] subjects [redacted] type I [redacted] (two-sided):

[redacted]

Sample Size Calculation 5

Clinical remission, obefazimod 50 mg versus placebo, difference [redacted] subjects [redacted] type I [redacted] (two-sided):

[redacted]

Sample Size Calculation 6

Endoscopic improvement, obefazimod 50 mg versus placebo, type I [redacted] (two-sided):

[redacted]

Sample Size Calculation 7

Endoscopic improvement, obefazimod 25 mg versus placebo, type I [redacted] (two-sided):

[redacted]

Sample Size Calculation 8

Symptomatic remission, obefazimod 50 mg versus placebo, type I [redacted] (two-sided):

[redacted]

Sample Size Calculation 9

Symptomatic remission, obefazimod 25 mg versus placebo, type I [redacted] (two-sided):

[redacted]

APPENDIX 2. PARTIAL DATE CONVENTIONS

Imputed dates will not be presented in the listings.

If the **date of UC diagnosis** is partial, missing day will be imputed with first day of the month and missing month will be imputed with January (for the purpose of deriving the **duration of UC**). If the date of UC diagnosis is completely missing, no imputation will be performed (and duration of UC will be missing).

If the **start date of an AE** is partial, day and/or month will be imputed in accordance with the following, for the purpose of deriving **exposure-adjusted incidence rates for AEs**:

- If both day and month of the AE start date are missing, the day and month will be imputed with the day and month of the first dose date, provided that the year is equal to the year of first dose. Otherwise, the month and day will be imputed as the first day of the year (01 Jan).
- If only day is missing, and if the year and month are equal to the first dose date, the day will be imputed as day of the first dose date. Otherwise, the day will be imputed as "01".
- If the **imputed start date of an AE** is after the stop date of the AE, the AE start day (and/or month) will be imputed to the 1st day of the month (1st day of the year) instead.

Treatment-emergence of AEs and **prior/concomitant medications** will be determined via the conventions described in Table G and Table H.

Table G: Algorithm for Treatment Emergence of AEs:

Start Date	Stop Date	Action
Known	Known/Partial/ Missing	If start date < study drug start date, then not TEAE If start date ≥ study drug start date, then TEAE
Partial, but known components show that it cannot be on or after study drug start date	Known/Partial/ Missing	Not TEAE
Partial, could be on or after study drug start date **or** Missing	Known	If stop date < study drug start date, then not TEAE If stop date ≥ study drug start date, then TEAE
	Partial	Impute stop date as latest possible date (i.e., last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study drug start date, then not TEAE If stop date ≥ study drug start date, then TEAE
	Missing	Assumed TEAE
Missing	Known	If AE stop date < study drug start date, then not TEAE If AE stop date ≥ study drug start date, then TEAE
	Partial	Impute AE stop date as latest possible date (i.e., last day of month if day unknown or 31st December if day and month are unknown), then: If AE stop date < study drug start date, then not TEAE If AE stop date ≥ study drug start date, then TEAE
	Missing	Assumed TEAE

Table H: Algorithm for Prior and Concomitant Medications:

Note: This does not apply to [redacted]

Start Date	Stop Date	Action
Known	Known	If stop date < study drug start date, assign as prior If stop date ≥ study drug start date assign as concomitant
	Partial	Impute stop date as latest possible date (i.e., last day of month if day unknown, December if month unknown, or 31st December if day and month are unknown), then: If stop date < study drug start date, assign as prior If stop date ≥ study drug start date assign as concomitant
	Missing	If stop date is missing could never be assumed a prior medication Assign as concomitant
Partial	Known	Impute start date as earliest possible date (i.e., first day of month if day unknown, January if month unknown, or 1st January if day and month are unknown), then: If stop date < study drug start date, assign as prior If stop date ≥ study drug start date assign as concomitant
	Partial	Impute start date as earliest possible date (i.e., first day of month if day unknown, January if month unknown, or 1st January if day and month are unknown) and impute stop date as latest possible date (i.e., last day of month if day unknown, December if month unknown, or 31st December if day and month are unknown), then: If stop date < study drug start date, assign as prior If stop date ≥ study drug start date assign as concomitant
	Missing	Impute start date as earliest possible date (i.e., first day of month if day unknown, January if month unknown, or 1st January if day and month are unknown), then: If stop date is missing could never be assumed a prior medication, assign as concomitant.
Missing	Known	If stop date < study drug start date, assign as prior If stop date ≥ study drug start date, assign as concomitant
	Partial	Impute stop date as latest possible date (i.e., last day of month if day unknown, December if month unknown, or 31st December if day and month are unknown), then: If stop date < study drug start date, assign as prior If stop date ≥ study drug start date, assign as concomitant
	Missing	Assign as concomitant

APPENDIX 3. PROGRAMMING CONVENTIONS FOR OUTPUTS

[redacted] Output Conventions
Outputs will be presented as shown in the Output shells and in accordance with the conventions described below.

Dates & Times
Depending on data available, dates and times will take the format of DDMMMYYYY:hh:mm.

Spelling Format
English US

Paper Size, Orientation, and Margins
The size of paper will be letter and the page orientation will be landscape. Margins will provide at least one inch (2.54 centimeters) of white space all around the page.

Fonts
Font type: 'Courier New'
Font size: 9
Font color: black

Sources
The source listing(s) and source dataset(s) will be included in the footnote of each table. The source table(s) and source dataset(s) will be included in the footnote of each figure. The source dataset(s) will be included in the footnote of each listing.

Presentation of Treatment Groups
For outputs, treatment groups will be represented as follows and in the given order:

Treatment Group	For Tables, Figures, and Listings (TLF)
ABX464 50 mg	ABX464 50 mg
ABX464 25 mg	ABX464 25 mg
Placebo	Placebo
Screen Failure	Screen Failure
Assigned, not treated	Assigned, not treated

Presentation of Visits
For outputs, visits will be represented as follows and in the given order:

Visit Name	Study Period
Screening	Screening
Baseline, Week 4, Week 8	Treatment
Safety Follow-Up	Follow-Up
Unscheduled	Unscheduled

Unless stated otherwise, listings will display CRF visit (rather than analysis visit). Within listings, 'Unscheduled' will appear in the 'Visit' column for assessments performed at unscheduled visits.

Data will be ordered by assessment/visit date (before visit name) – this way, visits (scheduled and unscheduled) will appear in chronological order.

Decimals, Percentages and P-values
Summary statistics should be displayed with the following number of decimal places, where N denotes the number of decimal places used for the source variable:

- Minimum and maximum: N
- Mean, median and CI: N+1
- SD, SE, LS Mean and CI of LS Mean: N+2
- SE of LS Mean: N+3
- Percentages will be reported to one decimal place. Where counts are zero, percentages will not appear in the output. Unless otherwise stated, percentages will be calculated out of the total population for each treatment group.
- OR and incidence rate per 100 subject-years of exposure will be reported to two decimal places.
- P-values will be reported to four decimal places, except values <1.000 but >0.9999 will be presented as '>0.9999' (e.g., 0.99998 is presented as >0.9999).
- Values <0.0001 will be presented as '<0.0001' (e.g., 0.00009 is presented as <0.0001). Rounding will be applied after the <0.0001 and >0.9999 rule.
- If statistics cannot be calculated due to limited data, 'NC' will be added to the output and the list of abbreviations in the table footnote.

Exceptions:

- A maximum of three decimal places will be displayed for all summary statistics (except p-values, as described above).
- All summary statistics will be reported to one decimal place for BMI.
- Three decimal places will be displayed for total exposure in the summary table of exposure adjusted incidence rates.

Listings
All listings will be ordered by the following (unless otherwise indicated in the template):

- Randomized treatment group (or treatment received if it's a safety output), first by active dose (by descending dose group) and then Placebo, then Screen Failure, then Assigned, not treated (if applicable).
- Subject Number (incorporating site number)
- Date (where applicable)
  Note: if assessment dates are missing, visits should be displayed in chronological order

APPENDIX 4. MMS SCORE AND SUBSCORE DERIVATIONS IN IRT

By-visit RBS and SFS values are calculated by the IRT using daily diary responses.

By-visit MMS values and the **MMS date** are also calculated by IRT.

The IRT-derivations of each of these values are described below.

The **daily RBS** is captured in the eDiary. This represents the most severe bleeding of the day, and is defined as follows:

- No blood seen=0
- Stool with streaks of blood=1
- Stool with more than streaks of blood=2
- Blood alone passed=3

The **daily SF** is captured in the eDiary. This is converted to a **daily SFS,** by subtracting the normal SF from the daily SF, in accordance with the following:

- Daily SFS=0 when daily SF–normal SF ≤0
- Daily SFS=1 when daily SF–normal SF=1 or 2
- Daily SFS=2 when daily SF–normal SF=3 or 4
- Daily SFS=3 when daily SF–normal SF ≥5

The normal SF is collected at the time of Screening.

By-visit SFS and RBS values for the Baseline and Week 8 /EoT visits are calculated by IRT using the daily RBS, daily SFS, and bowel preparation date, in accordance with the following rules:

- **Option 1** – If there is non-missing daily SFS and non-missing daily RBS data for at least three consecutive days in the 7 days prior to the date of bowel preparation, the by-visit SFS and RBS are each defined as the arithmetic mean of the daily SFS and daily RBS values (respectively) for the three consecutive days closest to the bowel preparation date*.
- **Option 2** – If option 1 is not met, and if there are non-missing daily SFS and non-missing daily RBS data for at least four non-consecutive days in the 7 days prior to the date of bowel preparation, the by-visit SFS and RBS are each defined as the arithmetic mean of the daily SFS and daily RBS values (respectively) for the four non-consecutive days closest to the bowel preparation date*.
- **Option 3** – If options 1 and 2 are not met, and if there are non-missing daily SFS and non-missing daily RBS data available on days 2, 3 and 4 post-endoscopy, the by-visit SFS and RBS are each defined as the arithmetic mean of the daily SFS and daily RBS values (respectively) for the three days post-endoscopy + 1 day*.

  If **no bowel preparation is performed at Week 8/EoT, then the IRT visit transaction date is used instead of the bowel preparation date for the above derivations, and option 3 is **not** considered/applied.*

The **date of MMS** is assigned as the bowel preparation date, unless the subject had NO endoscopy at Week 8/EoT, in which case the IRT visit transaction date is assigned.

By-visit SFS and by-visit RBS at the Screening visit are calculated by IRT using the daily SF and daily RBS data relative to the **Screening** bowel preparation date and using the three options outlined

above.

By-visit SFS and by-visit RBS for the pMMS at the Week 4 visit (where no endoscopy is done) are calculated analogously to the Baseline and Week 8 scores outlined above, although option 3 above is NOT considered/applied, and the Week 4 IRT visit transaction date is used instead of the bowel preparation date.

Notes:

- If more than one daily RBS or daily SF is reported in the eDiary for a given subject on a given day, IRT uses the latest of these for the above calculations.
- Derived by-visit SFS/RBS values are rounded by IRT, to the nearest integer (i.e., <0.5=0; ≥0.5=1).
- For Week 4, the **date of pMMS** is derived using the IRT visit transaction date - this date is also assigned to the associated Week 4 by-visit RBS and SFS.
- By-visit SFS and by-visit RBS are set to missing in IRT if subjects do not have sufficient daily diary data to fulfil one of the above specified options. As a result, the pMMS and MMS are also missing in this scenario.

APPENDIX 5. [redacted]

APPENDIX 6. GEBOES INDEX SCORE DERIVATION

Histology samples are analyzed by [redacted] For each subject and sample, [redacted] report the individual grade scores, per Table I:

Table I: Geboes Individual Grade Scores

Score	Grade
Grade 0: Architectural Changes	
0	No abnormality
1	Mild abnormality
2	Mild/moderate diffuse or focal abnormalities
3	Severe diffuse or multifocal abnormalities
Grade 1: Chronic Inflammatory Infiltrate	
0	No Increase
1	Mild but unequivocal increase
2	Moderate increase
3	Marked increase
Grade 2A: Eosinophils in Lamina propria	
0	No Increase
1	Mild but unequivocal increase
2	Moderate increase
3	Marked increase
Grade 2B: Neutrophils in Lamina propria	
0	No Increase
1	Mild but unequivocal increase
2	Moderate increase
3	Marked increase
Grade 3: Neutrophils in epithelium	
0	None
1	<5% crypts involved
2	<50% crypts involved
3	>50% crypts involved
Grade 4: Crypts destruction	
0	None
1	Probable: local excess of neutrophils in part of the crypts
2	Probable: marked attenuation
3	Unequivocal crypt destruction
Grade 5: Erosions and ulcerations	
0	No erosion, ulceration or granulation tissue
1	Recovering epithelium + adjacent inflammation
2	Probable erosion: focally stripped
3	Unequivocal erosion
4	Ulcer or granulation tissue

The Geboes Index score ranges from 0.0-5.4. The first digit reflects the highest grade with score >0. The second digit reflects the score for that grade. The Geboes Index score is zero when all grade

scores are zero.

[redacted]

APPENDIX 7. IBDQ SCORE DERIVATION

The IBDQ is a disease-specific instrument composed of 32 Likert-scaled items, each with seven response options (each scored from 1-7 points), which is completed at the Baseline visit and Week 8 visit. The IBDQ is provided in Appendix 3 of the Clinical Study Protocol.

The IBDQ scale contains four component dimensions: bowel symptoms, systemic symptoms, emotional function, and social function – the questions corresponding to each of these dimensions are detailed below (Guyatt G 1989):

- Bowel symptoms: Questions 1, 5, 9, 13, 17, 20, 22, 24, 26, 29
- Systemic symptoms: Questions 2, 6, 10, 14, 18
- Emotional health: Questions 3, 7, 11, 15, 19, 21, 23, 25, 27, 30, 31, 32
- Social function: Questions 4, 8, 12, 16, 28

Each dimension score can be computed by adding the scores for each of the items specified. Total dimension scores range from 10-70, 5-35, 12-84, and 5-35, respectively.

The individual IBDQ dimensions will be calculated when no more than one item is missing in the dimension. If an item is missing, it will be estimated using the average value across the non-missing items.

The IBDQ total score is the sum of the four individual dimension scores. If any of the four dimensions of the IBDQ cannot be calculated, then the total IBDQ score cannot be calculated.

The IBDQ total score ranges from 32-224, with higher scores indicating better health-related quality of life.

APPENDIX 8. EQ-5D-5L INDEX SCORE DERIVATION

The EQ-5D-5L is the 5-level version of the EQ-5D. The EQ-5D is designed for self-completion by subjects and consists of two parts – the EQ-5D descriptive system and the EQ Visual Analogue Scale. Subjects complete the EQ-5D Questionnaire at the Baseline visit, Week 4 visit and Week 8 visit.

The EQ-5D descriptive system comprises the following five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has five levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. Each of the five can be summed through a weighting system to generate the EQ-5D-5L Index score.

The second part of the EQ-5D-5L is a Visual Analogue Scale on which the subject rates their current health, with zero representing the "worst health you can imagine" and 100 representing the "best health you can imagine."

The EQ-5D-5L questionnaire is provided in Appendix 4 of the Clinical Study Protocol.

The EQ-5D-5L Index score is derived by mapping each domain answer to a weight, then summing these weights across all domains, and finally subtracting this total from 1.

The weights associated to each answer for each domain are presented in Table K (Pickard S 2019).

Table K: EQ-5D-5L Weights

Domain	Answer	Weight
Mobility	None	0
	Slight	0.096
	Moderate	0.122
	Severe	0.237
	Unable	0.322
Self-care	None	0
	Slight	0.089
	Moderate	0.107
	Severe	0.220
	Unable	0.261
Usual Activities	None	0
	Slight	0.068
	Moderate	0.101
	Severe	0.255
	Unable	0.255
Pain/discomfort	None	0
	Slight	0.060
	Moderate	0.098
	Severe	0.318
	Extreme	0.414
Anxiety/ depression	None	0

Domain	Answer	Weight
	Slight	0.057
	Moderate	0.123
	Severe	0.299
	Extreme	0.321

APPENDIX 9. FATIGUE NRS

Fatigue NRS is reported by the subject daily, via a single-item, 11-point horizontal scale anchored at zero and 10, with zero representing 'No fatigue' and 10 representing 'Fatigue as bad as you can imagine.' Subjects are asked to rate their fatigue (weariness, tiredness) by selecting the number that describes their worst level of fatigue during the past 24 hours.

The Baseline, Week 4 and Week 8 Fatigue NRS values are defined as the average of the NRS values entered over the closest three consecutive days or four non-consecutive days in the 7-day window before the Baseline, Week 4 and Week 8 clinic visits, respectively. The derived Fatigue NRS values will be rounded to the nearest integer. If three consecutive days or four non-consecutive days do not exist in the 7-day windows, Fatigue NRS will be missing. If both three consecutive days and four non-consecutive days with non-missing responses exist in the 7-day window, the three consecutive days will be used for the derivation.

APPENDIX 10. FACIT-FATIGUE SUBSCALE SCORING GUIDELINES

The FACIT-Fatigue subscale is a patient-reported 13-item questionnaire that assesses the subject fatigue in chronic diseases. Subjects complete the questionnaire at the Baseline and Week 8 visits.

The FACIT-Fatigue subscale is provided in Appendix 6 of the Clinical Study Protocol. The below scoring guidelines will be followed to derive the FACIT-Fatigue Subscale score for each subject and visit. If more than 50% of the responses are missing (i.e., more than 6 responses), the FACIT-Fatigue subscale score will be missing.

Instructions:

1. Record answers in "item response" column. If missing, mark with an X.
2. Perform reversals as indicated and sum individual items to obtain a score.
3. Multiply the sum of the item scores by the number of items in the subscale, then divide by the number of items answered. This produces the subscale score.
4. **The higher the score, the better the quality of life.**

Subscale	Item Code	Reverse Item?	Item Response	Item Score
FATIGUE SUBSCALE *Score Range:* 0-52	**HI7**	**4 -**	_____	= _____
	HI12	**4 -**	_____	= _____
	An1	**4 -**	_____	= _____
	An2	**4 -**	_____	= _____
	An3	**4 -**	_____	= _____
	An4	**4 -**	_____	= _____
	An5	**0 +**	_____	= _____
	An7	**0 +**	_____	= _____
	An8	**4 -**	_____	= _____
	An12	**4 -**	_____	= _____
	An14	**4 -**	_____	= _____
	An15	**4 -**	_____	= _____
	An16	**4 -**	_____	= _____

Sum individual item scores: _____
Multiply by 13: _____
Divide by number of items answered: _____
= **Fatigue Subscale Score**

APPENDIX 11. WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT QUESTIONNAIRE: ULCERATIVE COLITIS (WPAI:UC)

The WPAI:UC questionnaire measures impairments in both paid work and unpaid work. A copy of the questionnaire is provided in Appendix 5 of the Clinical Study Protocol. It consists of six questions:

- Q1 = currently employed;
- Q2 = hours missed due to UC;
- Q3 = hours missed for other reasons;
- Q4 = hours actually worked;
- Q5 = degree UC affected productivity while working;
- Q6 = degree UC affected productivity in regular unpaid activities.

Subjects complete the WPAI:UC questionnaire at the Baseline visit and Week 8 visit.

Four main outcomes are generated from the WPAI:UC. These will be derived as follows:

- percent work time missed due to UC: Q2/(Q2+Q4)
- percent impairment while working due to UC: Q5/10
- percent overall work impairment due to UC: Q2/(Q2+Q4)+[(1-(Q2/(Q2+Q4)))*(Q5/10)]
- percent activity impairment due to UC: Q6/10

Note: Each of the above scores should be multiplied by 100 to express as percentages.

APPENDIX 12. LABORATORY-RELATED ADVERSE EVENTS (AEs)

Adverse events which are coded to any of the below specified system organ class and PT combinations, will be considered laboratory-related AEs.

Table L: Laboratory Related Adverse Events (AEs)

System Organ Class (SOC) Preferred Term (PT)
Blood and lymphatic system disorders
Anaemia
Blood loss anaemia
Deficiency anaemia
Iron deficiency anaemia
Basophilopenia
Eosinopenia
Hyperfibrinogenaemia
Hyperprothrombinaemia
Hypofibrinogenaemia
Hypoprothrombinaemia
Leukocytosis
Leukopenia
Lymphopenia
Monocytopenia
Neutropenia
Neutrophilia
Thrombocytopenia
Hepatobiliary disorders
Hyperbilirubinaemia
Investigations
Alanine aminotransferase abnormal
Alanine aminotransferase increased
[redacted]
Aspartate aminotransferase abnormal
Aspartate aminotransferase increased
Basophil count abnormal
Basophil count decreased
Basophil count increased
Blood albumin abnormal
Blood albumin decreased
Blood albumin increased

Blood alkaline phosphatase abnormal
Blood alkaline phosphatase increased
Blood bilirubin abnormal
Blood bilirubin increased
Blood calcium
Blood calcium abnormal
Blood calcium decreased
Blood chloride abnormal
Blood chloride decreased
Blood chloride increased
Blood cholesterol abnormal
Blood cholesterol increased
Blood creatine phosphokinase abnormal
Blood creatine phosphokinase increased
Blood fibrinogen abnormal
Blood fibrinogen decreased
Blood fibrinogen increased
Blood follicle stimulating hormone abnormal
Blood follicle stimulating hormone decreased
Blood follicle stimulating hormone increased
Blood lactate dehydrogenase abnormal
Blood lactate dehydrogenase decreased
Blood lactate dehydrogenase increased
Blood magnesium abnormal
Blood magnesium decreased
Blood magnesium increased
Blood phosphorus abnormal
Blood phosphorus decreased
Blood phosphorus increased
Blood potassium abnormal
Blood potassium decreased
Blood potassium increased
Blood sodium abnormal
Blood sodium decreased
Blood sodium increased
Blood triglycerides abnormal
Blood triglycerides increased
C-reactive protein abnormal
C-reactive protein decreased
C-reactive protein increased
Creatinine renal clearance abnormal
Creatinine renal clearance decreased

Creatinine renal clearance increased
Eosinophil count abnormal
Eosinophil count decreased
Eosinophil count increased
Gamma-glutamyltransferase abnormal
Gamma-glutamyltransferase increased
Granulocyte count
Granulocyte count decreased
Granulocyte count increased
Haematocrit abnormal
Haemoglobin decreased
Haemoglobin increased
Hepatic enzyme abnormal
Hepatic enzyme increased
High density lipoprotein abnormal
High density lipoprotein decreased
High density lipoprotein increased
Human chorionic gonadotropin increased
Human chorionic gonadotropin positive
International normalised ratio abnormal
International normalised ratio decreased
International normalised ratio increased
[redacted]
Lipids abnormal
Lipids increased
Lipoprotein abnormal
Lipoprotein increased
Liver function test abnormal
Liver function test increased
Low density lipoprotein abnormal
Low density lipoprotein decreased
Low density lipoprotein increased
Lymphocyte count abnormal
Lymphocyte count decreased
Lymphocyte count increased
Monocyte count abnormal
Monocyte count decreased
Monocyte count increased
Neutrophil count abnormal
Neutrophil count decreased
Neutrophil count increased

[redacted]
Platelet count abnormal
Platelet count decreased
Platelet count increased
Protein total abnormal
Protein total decreased
Protein total increased
Prothrombin level abnormal
Prothrombin level decreased
Prothrombin level increased
Red blood cell count abnormal
Red blood cell count decreased
Red blood cell count increased
Transaminases abnormal
Transaminases increased
[redacted]
Very low density lipoprotein abnormal
Very low density lipoprotein decreased
Very low density lipoprotein increased
White blood cell count abnormal
White blood cell count decreased
White blood cell count increased

Metabolism and nutrition disorders

Dyslipidaemia
Hyper HDL cholesterolaemia
Hyperalbuminaemia
[redacted]
Hypercalcaemia
Hypercholesterolaemia
Hypercreatininaemia
Hyperglycaemia
Hyperkalaemia
[redacted]
Hyperlipidaemia
Hypermagnesaemia
Hypernatraemia
Hyperphosphataemia
Hyperproteinaemia

Hypertriglyceridaemia
Hypo HDL cholesterolaemia
Hypoalbuminaemia
Hypocalcaemia
Hypocholesterolaemia
Hypoglycaemia
Hypokalaemia
Hypolipidaemia
Hypomagnesaemia
Hyponatraemia
Hypophosphataemia
Hypoproteinaemia
Hypotriglyceridaemia
Lipoprotein deficiency
Magnesium deficiency

Musculoskeletal and connective tissue disorders

Hypercreatinaemia

APPENDIX 13. CLASSIFICATION OF RESCUE THERAPY

This appendix outlines the algorithm for the Abivax clinical/medical reviewers to classify prohibited concomitant medications for UC, which impact efficacy, in a blinded manner. This will help establish IEs (IE #2) for the efficacy estimands. All prohibited concomitant medications identified by the reviewers, per the algorithm below, will be imported into the analysis datasets. The process will be repeated until database lock, and the list of all prohibited medications identified will be finalized before study unblinding.

Only medications reported on the eCRFs can be assessed. If the exposure happens in the follow-up period (beginning on or after the date of last study treatment), then it would not be considered an IE. The rules outlined below apply to both new use and increase in dose from Baseline.

Medication Type	Considerations for Efficacy Endpoints	List of Medications	Routes
5-ASA Compounds	• Existing medication: Any increase from Baseline for more than 5 days OR within 2 weeks prior to endoscopy • New medication: Any exposure during the treatment period and prior to Week 8 Endoscopy	• BALSALAZIDE • BALSALAZIDE DISODIUM DIHYDRATE • BALSALAZIDE SODIUM • OLSALAZINE SODIUM • BECLOMETASONE W/MESALAZINE • MESALAZINE	• Oral • Buccal • Rectal
Corticosteroids	• Existing medication: Any increase from Baseline for more than 5 days OR within 2 weeks prior to endoscopy • New medication: Any exposure during the treatment period and prior to Week 8 Endoscopy	• BECLOMETHASONE • BECLOMETHASONE DIPROPIONATE • BUDESONIDE • DEXAMETHASONE • DEXAMETHASONE SODIUM PHOSPHATE • DEXAMETHASONE VALERATE • HYDROCORTISONE • HYDROCORTISONE ACETATE • HYDROCORTISONE BUTYRATE • HYDROCORTISONE SODIUM SUCCINATE • MEPREDNISONE	• Oral • Buccal • Intravenous • Intramuscular • Rectal • Enema (identified via Other Route specified)

		• METHYLPREDNISOLONE • METHYLPREDNISOLONE SODIUM SUCCINATE • PREDNISOLONE • PREDNISOLONE ACETATEPREDNISOLONE SODIUM PHOSPHATE • PREDNISOLONE METASULFOBENZOATE SODIUM • PREDNISONE • PREDNISONE ACETATE • TRIAMCINOLONE	
Immuno-suppressants	New medication: Any exposure during the treatment period	• 6-MERCAPTOPURINE • AZATHIOPRINE • CYCLOSPORIN • METHOTREXATE • METHOTREXATE SODIUM • TACROLIMUS • TIOGUANINE	• Oral • Intravenous • Subcutaneous • Intramuscular
Advanced Therapies	New medication: Any exposure during the treatment period	• ADALIMUMAB (or Biosimilar) • CERTOLIZUMAB • CERTOLIZUMAB PEGOL • ETRASIMOD • FILGOTINIB • GOLIMUMAB • INFLIXIMAB (or Biosimilar) • MIRIKIZUMAB • NATALIZUMAB • OZANIMOD • RISANKIZUMAB • TOFACITINIB • VEDOLIZUMAB • UPADACITINIB • USTEKINUMAB (or Biosimilar)	Any
[redacted]	New medication: Any exposure during the treatment period	[redacted]	• Oral • Intravenous
Anti-diarrheals	New medication: Any exposure during the treatment period >7 days AND within 2 weeks prior to endoscopy	Any medication with ATC Level 4 of one of the following: • ANTIDIARRHEAL MICROORGANISMS • ANTIPROPULSIVES	Oral

		• OTHER INTESTINAL ADSORBENTSOTHER ANTIDIARRHEALS	
NSAIDs	New medication: Any exposure during the treatment period >7 days AND within 2 weeks prior to endoscopy	• ACETYLSALICYLIC ACID • CELECOXIB • DICLOFENAC • DICLOFENAC DIETHYLAMINE • DICLOFENAC;PARACETAMOL • DIFLUNISAL • ETODOLAC • FENOPROFEN • FLURBIPROFEN • IBUPROFEN • INDOMETHACIN • KETOPROFEN • KETOROLAC • MEFENAMIC ACID • MELOXICAM • NABUMETONE • NAPROXEN • NIMESULIDE • OXAPROZIN • PIROXICAM • SULINDAC	• Oral • Intravenous

For medications already in use during screening (e.g., 5-ASA, glucocorticoids), the highest dose taken prior to the date of first dose of study treatment will be considered in assessing ‘any increase from Baseline’.