STATISTICAL ANALYSIS PLAN

ABX464-103

A randomized, double blind, placebo controlled, parallel group, multiple dose, induction study to evaluate the safety, tolerability and optimal dose of ABX464 compared with placebo in patients with moderate to severe ulcerative colitis who have inadequate response, loss of response, or intolerance with at least one of the following agents: immunosuppressant treatment (i.e. azathioprine, 6-mercaptopurine, methotrexate), tumor necrosis factor alpha [TNF-α] inhibitors, vedolizumab, JAK inhibitors and/or corticosteroid treatment.

ABX464-103 is a Phase IIb study.

[redacted]

Version Number and Date: V2.0 10May2021

Statistical Analysis Plan Signature Page

Statistical Analysis Plan V2.0 (Dated 10 May 2021) for Protocol ABX464-103 version 3.0, dated 22 June 2020.

	Name	**Signature**	**Date** DDMMMYYYY
Author:	[redacted]	*Refer to electronic signature*	
Position:	[redacted]		
Company:	IQVIA		

Upon review of this document, the undersigned approves this version of the Statistical Analysis Plan, authorizing that the content is acceptable for the reporting of this study.

	Name	**Signature**	**Date** DDMMMYYYY
Approved By:	[redacted]	*Refer to electronic signature*	
Position:	[redacted]		
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Modification History

Unique Identifier for this Version	Date of the Document Version	Author	Significant Changes from Previous Authorized Version
1.0	3 August 2020	[redacted]	Not Applicable – First Version
2.0	5 May 2021	[redacted]	1. Section 2.3 Estimands updated for Intercurrent event handling strategy. 2. Section 3.3 Changes to Analysis from protocol updated. 3. Section 5.1 & 5.2.4 Blind Data Review and Per Protocol Analysis set updated 4. Section 7.1 Adjustments For Covariates And Factors To Be Included In Analyses updated 5. Section 7.2 Multicenter Studies 6. Section 7.3 Missing Data 7. Section 7.4 Multiple Comparisons/Multiplicity 8. Section 7.5 Examination Of Subgroups updated 9. Section 10 Demographic And Other Baseline Characteristics updated 10. Section 10.1.2 Time since stopping tobacco usage (former smokers) updated 11. Section 10.1.4 Time Since Diagnosis Of Ulcerative Colitis updated. 12. Section 12 Prior And Concomitant Medications updated 13. Section 13 Study Medication Exposure updated 14. Section 13.1 Derivations

			15. Section 14 Study Medication Compliance updated 16. Section 15.1.2 Missing Data Methods For Primary Efficacy Variable updated 17. Section 15.1.3 Primary Analysis Of Primary Efficacy Variable updated 18. Section 15.1.4.1 Confirmation of analysis results updated as Per Protocol Analyses. 19. Section 15.1.4.2 Sensitivity to Subgroup Analysis updated 20. Section 15.2 Secondary Efficacy updated 21. Section 15.2.1 Secondary Efficacy Variables & Derivations including subsections updated 22. Section 15.2.2 Missing Data Methods For Secondary Efficacy Variable(S) updated 23. Section 15.2.3 Analysis of Secondary Efficacy Variables and subsections updated 24. Section 16 Pharmacokinetics updated 25. Section 17.2 Laboratory Evaluations updated 26. Section 17.3 ECG Evaluations updated 27. Section 17.4 Vital Signs updated 28. Section 18 References updated 29. Appendix 1 Programming Conventions for Outputs updated 30. Appendix 4 SAS® Code removed 31. Appendix 4 Geboes Score Components added 32. Appendix 5 Concomitant UC medication added

LIST OF ABBREVIATIONS

AE	adverse event
AESI	adverse event of special interest
ALT/SGPT	alanine aminotransferase/serum glutamic pyruvate transaminase
ANCOVA	analysis of covariance
AR	autoregressive
AST/SGOT	aspartate aminotransferase/serum glutamic oxaloacetic transaminase
ATC	Anatomical Theoretical Chemical
BDR	Blind Data Review
BLQ	below the lower limit of quantification
BMI	Body Mass Index
bpm	beats per minute
CI	Confidence Interval
CM	concomitant medicine
CMV	Cytomegalovirus
CNS	Central Nervous System
CONS	All Subjects Consented Analysis Set
CRF	Case Report Form
CRT	Core Review Team
CRP	C-Reactive Protein
CS	clinically significant
CTC-AE	Common Terminology Criteria for Adverse Events, version 4.0
CTMS	Clinical Trial Management System
DA	drug accountability
DBL	database lock
DBP	Diastolic Blood Pressure
DHD	data handling database
DM	demography
DOV	day of visit
DSMB	Data and Safety Monitoring Board
DTL	data team lead
EC	exposure
ECG	electrocardiogram
ECCO	European Crohn's and Colitis Organisation
EDTA	ethylenediaminetetraacetic acid
EOS	end of study
FAS	Full Analysis Set
HR	heart rate
IBD	Inflammatory Bowel Disease
IBDQ	Inflammatory Bowel Disease Questionnaire
ICF	informed consent form
ICH	International Conference on Harmonization
IL-22	InterleukiIL-22ne 22
JAK	Janus Kinase
LLT	lower level term
LOCF	Last Observation Carried Forward

Max	maximum
MedDRA	Medical Dictionary for Regulatory Activities
mg	milligram
MH	medical history
Min	minimum
miR	micro-RNA
mL	milliliter
mmHg	millimeters of mercury
MMRM	Mixed Model Repeated Measures
MMS	Modified Mayo Score
msec	millisecond
MW	medical writing
NCS	not clinically significant
o.d.	Once Daily
PCSA	potentially clinically significant abnormalities
PD	pharmacodynamics
PD	protocol deviation
PK	pharmacokinetics
PL	project lead
pMMS	Partial Modified Mayo Score
PPAS	Per Protocol Analysis Set
PR	procedure history
PREG	pregnancy test
PT	Preferred Term
QA	quality assurance
QC	quality control
QoL	Quality of Life
RHI	Robarts Histopathology Index
RNA	ribonucleic acid
SAE	serious adverse event
SAF	Safety Analysis Set
SAP	Statistical Analysis Plan
SBP	systolic blood pressure
SD	standard deviation
SEM	standard error of the mean
SOC	system organ class
STL	Statistics team lead
TB	Tuberculosis
TEAE	treatment emergent adverse event
TMS	Total Mayo Score
TNF	Tumor Necrosis Factor
TOEP	Toeplitz
UC	Ulcerative Colitis
UCHX	Ulcerative colitis history
ULN	Upper Limit Normal
ULQ	upper limit of quantification
VR	ventricular rate
WHO	World Health Organization

Table of Contents

1. INTRODUCTION

This document describes the rules and conventions to be used in the presentation and analysis of efficacy and safety data for protocol ABX464-103. It describes the data to be summarized and analysed, including specifics of the statistical analyses to be performed.

This statistical analysis plan (SAP) is based on protocol version 3.0, dated 22 June 2020.

2. STUDY OBJECTIVES

2.1. PRIMARY OBJECTIVE

The primary objective of this study is to determine an optimal ABX464 dose to be used in moderate to severe active ulcerative colitis patients who have failed or are intolerant to immunomodulators, anti-Tumor Necrosis Factor-α (TNF- α), vedolizumab, Janus Kinase (JAK) inhibitors and/or corticosteroids by comparing the mean change from baseline in the Modified Mayo Score (MMS) at Week 8 between each ABX464 group and placebo.

2.2. SECONDARY OBJECTIVES

The secondary objectives are:

- To evaluate the effect of the different dose groups of ABX464 versus placebo on:
    - MMS at Week 16 (if available) and on partial Modified Mayo Score (pMMS) at every study visit
    - Clinical remission at Week 8 and at Week 16 (if available)
    - Clinical response at Week 8 and at Week 16 (if available)

- Endoscopic improvement and endoscopic remission, by segment, at Week 8 and Week 16 (if available)
- Mucosal healing at Week 8 and Week 16 (if available)
- Stool and rectal bleeding frequency at every study visit
- Fecal calprotectin and C-reactive Protein (CRP) levels at Week 8 and Week 16
- miR-124 expression in tissue (Ribonucleic Acid (RNA) later) at Week 8 and Week 16 (if available) and in total blood at every timepoint
- Rectal/sigmoidal infiltrates using the Robarts Histopathology Index (RHI), the Geboes and Nancy Histology Scoring Scales at Week 8 and Week 16 (if available)
- Quality of Life (QoL) measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) at Week 8 and Week 16
- IL-6, TNFα, IL-1b, IL-10 plasma concentrations at every timepoint

- To evaluate the global effect of ABX464 on MMS at Week 8 and Week 16 (if available) and on pMMS at every study visit versus placebo
- To assess the pharmacokinetics of ABX464 and its main active metabolite ABX464-N_Glu after oral administration of different daily doses of ABX464 using population approach
- To evaluate the safety profile of the different dose groups of ABX464 versus placebo.

2.3. ESTIMANDS

The primary and secondary estimands to support regulatory decisions are described in Table A below. The intercurrent event is the early discontinuation of patients from the study and/or missing Week 8 efficacy assessments.

Table A List of Estimands

Estimand	Definition	Attributes			
		Population	**Variable/Endpoint**	**Intercurrent event handling strategy**	**Population-level summary measure**
Primary	Optimal ABX464 dose	All patients randomized, received at least one dose of study drug and provided at least one efficacy data point	Mean change in MMS from baseline to Week 8	Missing Week 8 MMS components (stool frequency, rectal bleeding and endoscopy subscores) will be imputed using methods detailed in section 7.3.	Mean change from baseline
Secondary	The effect of different dose groups vs placebo on secondary variables	All patients randomized, received at least one dose of study drug and provided at least one efficacy data point	Mean change from baseline to Weeks 8 and 16 in pMMS	Missing Week 8 pMMS components (stool frequency and rectal bleeding subscores) will be imputed using methods detailed in section 7.3.	Mean change from baseline
			Clinical remission or response at Weeks 8 and 16	Patients with missing Week 8 assessment will be considered non-responders	Proportion of responders in each treatment group
			Mean change from baseline to Week 8 in fecal calprotectin and CRP levels	Missing fecal calprotectin and CRP values will not be imputed.	Mean change from baseline

3. STUDY DESIGN

3.1. GENERAL DESCRIPTION

This is a randomized, double blind, placebo controlled, parallel group, multiple dose, induction study to evaluate the safety, tolerability of ABX464 compared with placebo in patients with moderate to severe ulcerative colitis who have inadequate response, loss of response, or intolerance with at least one of the following agents: immunosuppressant treatment (i.e. azathioprine, 6-mercaptopurine, methotrexate), TNF-α inhibitors, vedolizumab, JAK inhibitors and/or corticosteroid treatment. This phase IIb study will evaluate the efficacy and the safety of three dose-levels of ABX464, administered daily, in improving MMS in patients at Week 8.

Approximately 244 patients from 110 to 150 sites in Europe, Canada and United States of America (US) will participate in this study. Eligible patients from non-US sites will be randomized 1:1:1:1 into four parallel intervention/treatment groups as described in Table B. Patients in the US will be randomized 1:1:1 to 25 mg, 50 mg and placebo treatment groups. Approximately 61 patients will be randomized to each study treatment arm.

Table B Treatment Groups

Intervention/treatment Active Arm	
Group #1: 25mg once daily (q.d)	1 capsule of 25mg ABX464 + 1 capsule of Placebo
Group #2: 50mg q.d	1 capsule of 50mg ABX464 + 1 capsule of Placebo
Group #3: 100mg q.d	2 capsules of 50mg ABX464
Group #4: Placebo q.d	2 capsules of Placebo

Randomization will be stratified by:

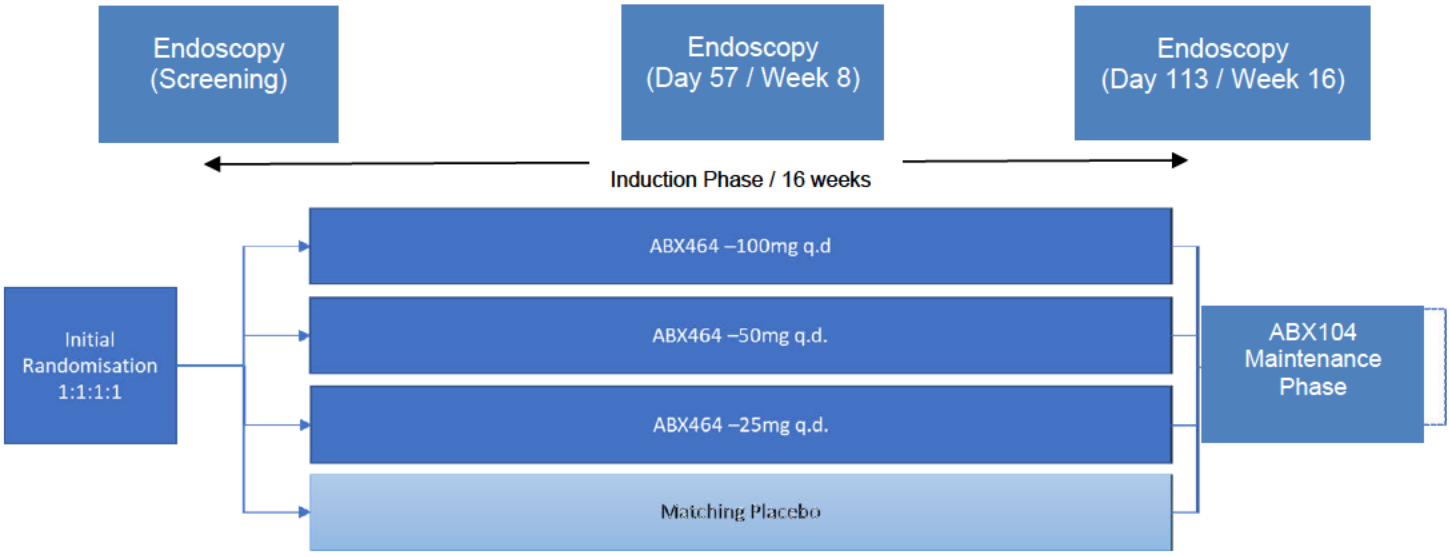
- US vs non-US patients
- Previous exposure and non-exposure to biological drugs or JAK inhibitors.

The proportion of patients with previous exposure to biologics or JAK inhibitors will be limited to 60%; including a maximal proportion of patients with previous treatment with vedolizumab of 20%. The maximal proportion of patients with previous exposure to JAK inhibitors will be limited to 10%.

Patients will be treated for 16 weeks in this induction study. All endoscopies (videos) will be centrally reviewed. E-Diaries will be used to collect frequency of stools, rectal bleedings, number of capsules taken and the intake time.

Flexible sigmoidoscopy with rectal and/or sigmoidal biopsies will be performed at screening, at Day 57 +/- 4 days (Week 8) and at Day 113 +/-4 days (Week 16). The Day 113 measurement will only be taken if the patient does not experience endoscopic improvement (i.e. endoscopy sub-score of 2 or 3) at Day 57. In the event of clinical progression of the disease after Week 8, defined as at least a 2-point increase from screening in pMMS, with a MMS $\geq$ 4 confirmed by an endoscopy sub score of 2 points or higher, the patient will exit the study.

Study Design



3.2. SCHEDULE OF EVENTS

Schedule of events can be found in Section 5.1 of the protocol.

3.3. CHANGES TO ANALYSIS FROM PROTOCOL

The FAS population will include subjects who received at least one dose of study treatment, and who have baseline data for at least one efficacy variable.

Descriptive statistics for electrocardiogram (ECG) parameters will not be calculated as per protocol. Individual parameter results will be kept on site, but only the number of patients with normal, abnormal - not clinically significant (NCS) and abnormal - clinically significant (CS) results will be reported. Potentially Clinically Significant Abnormalities (PCSA) will not be considered due to data unavailability.

The Country and US vs Non-US subgroup analyses will not be performed because of the small number of subjects from some countries.

Analyses of miRNA-124 levels in blood and tissue will be analysed and reported separately by an independent vendor and will be excluded from the final outputs and analysis conducted by IQVIA. Additionally, pharmacokinetic (PK) results will also be reported separately by an independent vendor, but external data may be made available to IQVIA Biostatistics and the subgroup 'Week 16 ABX464-NGlu AUC0-12 level above/below 7 000 h*ng/mL' will be included in subgroup analyses, if available.

The analysis of the following secondary endpoints will not be addressed in this SAP:

- Change relative to baseline in miRNA-124 expression
- Change relative to baseline in infiltrate/histopathology (Sigmoidal) using the RHI
- IL-6, TNFα, IL-1b, IL-10 plasma concentrations
- Serum concentration of ABX464 and N-Glucuronide ABX464

4. PLANNED ANALYSES

The following analyses will be performed for this study:

- Analyses for Data Safety Monitoring Board (DSMB) meetings
- Final Analysis

4.1. DATA SAFETY MONITORING BOARD (DSMB)

A DSMB will review the safety of the trial every two months during the entire study period. A DSMB charter describing the methodology and presentation of results and access to results will be provided by Abivax as a separate document.

4.2. INTERIM ANALYSIS

There will be no interim analysis for this study.

4.3. FINAL ANALYSIS

All final, planned analyses identified in this SAP will be performed by IQVIA Biostatistics following Sponsor Authorization of this SAP, Sponsor Authorization of Analysis Sets, Database Lock (DBL) and Unblinding of Treatment.

5. ANALYSIS SETS

Agreement and authorization of patients included/excluded from each analysis set will be conducted prior to the unblinding of the study. To facilitate this, a Blind Data Review (BDR) of data will be co-ordinated by the IQVIA Statistical Team Lead (STL).

5.1. BLIND DATA REVIEW PROCESS

This process comprises the timely collection and distribution of all relevant data review deliverables. The facilitation of final BDR meeting prior to DBL of all safety and efficacy data and deliverables is also included in the BDR process.

The Core Review Team (CRT) will comprise, at a minimum, the persons in **Table C** in their stated capacities. It remains the individual CRT's responsibility to choose whether additional participants will be required. If any other persons (Abivax or IQVIA) will participate in the data review process, they will be required to review the necessary documentation as set out later in this section.

Table C: Core Review Team of Blinded Safety and Efficacy Data

Role	Organization
Blinded Statistical Team Lead (STL)	IQVIA
Clinical Project Manager (CPM)/Project Lead (PL)	IQVIA
Medical Advisor (MA)	IQVIA
Data Team Lead (DTL)	IQVIA
Project Coordinator	Abivax
VP, Clinical Operations	Abivax
Chief Medical Officer (CMO)	Abivax
Principal Co-ordinating Investigator	Universitair Ziekenhuis Leuven

[redacted]

Table D Blind Data Review Meetings indicates the estimated timeframe for each planned data review meeting, format of meeting and expected status of the data. It should be noted that the information below

is an estimation and may be subject to change:

Table D Blind Data Review Meetings

Data Review Meeting	Estimated Meeting Time Frame	Format of Meeting and Status of Data Received
Final	[redacted]	Clean snapshot of the data will be used. Data review documents will be sent to the CRT before the meeting. Analysis set assignment will be performed.

[redacted]

[redacted]

Any exceptions to the analysis set assignments described in Section 5.2 will be reviewed on an individual basis.

5.2. ANALYSIS SETS

5.2.1. ALL PATIENTS CONSENTED ANALYSIS SET [CONS]

The All Patients Consented (CONS) Analysis Set will contain all patients who provided written informed consent (IC) to the study.

The following patients will be excluded from this Analysis Set:

- Patients who did not provide written informed consent at the screening visit

CRITERION [1]: No Written Informed Consent Provided.
DEVIATION STATUS: Major.
NOTES: • Data for all patients (including screen failures considered not eligible for enrollment) will be entered into the clinical study database and made available for presentation. • Data for rescreened patients are analyzed as assigned to the new patient number only. No data will be transferred from a previous data patient number to the new patient number. All baseline data required per the protocol will be collected under the new patient number. • This criterion will be tested using: • The date that informed consent was signed, as captured on the Demography (DM) eCRF and obtained from raw.DSSTDAT_IC.

5.2.2. SAFETY ANALYSIS SET [SAF]

The Safety Analysis Set (SAF) will include all randomized patients who have received at least one dose of the study treatment. If there is any doubt whether a patient was treated or not, they will be assumed treated for the purposes of analysis. The SAF will be used for all safety analyses and patients will be analyzed as treated. Should a subject be exposed to two different treatment doses during the study, the subject will be analyzed according to the treatment received most of the time. This will be confirmed on

a case-by-case basis at the BDR meeting.

The following patients will be excluded from this Analysis Set:

- Patients who have not received at least one dose of the study treatment:

CRITERION [3]: Randomized but no dose of ABX464 or Placebo Taken
DEVIATION STATUS: Major.

NOTES:
• This criterion will be tested using the following data, as captured on the Exposure (EC) and drug accountability (DA) eCRF:
  • The start date of study medication, as obtained from raw.EC.ECSTDAT.
  • Number of capsules dispensed and returned, as obtained from raw.DA.DAORRES4 and DAORRES5.

5.2.3. FULL ANALYSIS SET [FAS]

The Full Analysis Set (FAS) will include all patients included in the study who have received at least one dose of the study treatment, and who have baseline data for at least one efficacy variable.

The following patients will be excluded from this Analysis Set:

- All patients excluded from the SAF
- All patients who do not have baseline data for at least one efficacy variable

CRITERION [4]: Does not have baseline data for at least one efficacy variable
DEVIATION STATUS: Major.
NOTES: • This criterion will be tested using the following data, as captured in the eCRF and e-Diaries: • Baseline MMS and pMMS as obtained from raw.MMS.MMSSCR and raw.PMMS.PMMSSCR, prior to first dose of study treatment. Baseline stool frequency (raw.MMS.MMSST), rectal bleeding frequency

(raw.MMS.MMSRB) and endoscopic assessments (raw.MMS.MMSMA) will also be obtained from these scores. • Baseline fecal calprotectin and CRP levels as obtained from the laboratory. • Baseline IBDQ questionnaire completed as captured in the eDiary.

5.2.4. PER PROTOCOL ANALYSIS SET [PPAS]

The Per Protocol Analysis Set (PPAS) will include all patients in the FAS who do not have major PDs that would affect the evaluation of the primary efficacy endpoint. From a statistical analysis perspective, the reason(s) for exclusion of patients may be a PD or other factors affecting the primary efficacy outcome. PDs identified during the clinical conduct of the study, as authorized in the final PD log, will also be taken into consideration in the final assignment of patients to the analysis sets.

Reasons for exclusion are defined as:

- Insufficient essential efficacy data i.e. no MMS score at either Baseline or Week 8
- Non-compliance with the inclusion or exclusion criteria, including insufficient evidence of the study indication, i.e. MMS score < 5 (or MMS < for patients enrolled on original protocol) and endoscopy sub-score < 2 at screening
- Non-compliance with the study treatment up to Week 8 (< 80%)
- Intake of prohibited medication up to Week 8
- Non-compliance with time window up to Week 8 (+/- 7 days) (to be confirmed at CRT meeting)

Therefore, the following patients will be excluded from this Analysis Set:

- All patients excluded from the FAS.
- Patients with essential efficacy data missing or invalid:

CRITERION [5]: Insufficient Essential Efficacy Data
DEVIATION STATUS: Major.
NOTES:

- The primary efficacy variable is the change in MMS score from baseline to Week 8.
- This criterion will be tested using:
    - The subject's MMS scores, as captured on the MMS eCRF and obtained from raw.MMS.MMSSCR at Week 8.

- Patients with insufficient evidence of the study indication, i.e. ulcerative colitis:

CRITERION [6]: Insufficient Evidence of the Study Indication
DEVIATION STATUS: Major/No Major Impact, to be decided on a case-by-case basis at the final data review meeting.
NOTES: • This criterion will be tested at Screening, and not meeting the following criteria will be captured on the IE eCRF by raw.IE.IECAT and IETESTCD, as well as on the MMS eCRF by raw.MMS.MMSSCR and raw.MMS.MMSMA: • The subject must have a clinically confirmed diagnosis of moderate to severe ulcerative colitis, with an MMS score of 5 to 9 inclusive and endoscopy sub-score of at least 2. Subjects enrolled on original protocol may have a baseline MMS score of 4.

- Patients younger than 18 or older than 75 years:

CRITERION [7]: Patients Younger than 18 or older than 75 Years
DEVIATION STATUS: Major/No Major Impact, to be decided on a case-by-case basis at the final data review meeting.

NOTES:
• Age (years) as at informed consent will be used.
• This criterion will be tested using:
  • The date of birth as captured on the Demographics (DM) eCRF and obtained from raw.DM.BRTHDATZ and raw.DM.AGE.
  • The date of informed consent as captured on the DM eCRF and obtained from

raw.DM.DSSTDAT_IC.

- Patients who didn't meet the required laboratory screening criteria:

CRITERION [8]: Patient Didn't Meet Laboratory Screening Criteria
DEVIATION STATUS: Major/No Major Impact, to be decided on a case-by-case basis at the final data review meeting.

NOTES:
• The patient must meet the following laboratory screening criteria:
  • Haemoglobin > 9 g/dL^{-1}
  • Absolute neutrophil count ≥ 750 mm-3
  • Platelets ≥ 100,000 mm-3
  • Total serum creatinine ≤ 1.3 x ULN (upper limit of normal)
  • Creatinine clearance > 90 mL min-1 by the Cockcroft-Gault equation within 60 days prior to baseline
  • Total serum bilirubin < 1.5 x ULN
  • Alkaline phosphatase, aspartate aminotransferase (AST)/serum glutamic oxaloacetic transaminase (SGOT) and alanine aminotransferase (ALT)/serum glutamic pyruvate transaminase (SGPT) < 2 x ULN
• This criterion will be tested using the following data:
  • Not meeting these criteria will be captured on the IE eCRF and obtained from raw.IE.IEYN, IECAT and IETESTCD.

- Patients who didn't have documented inadequate response, no response, loss of response or an intolerance to specified alternate treatments:

• CRITERION [9]: Patient Didn't have Documented Inadequate Response, No Response, Loss of Response or an Intolerance to Specified Alternate Treatments:
DEVIATION STATUS: Major/No Major Impact, to be decided on a case-by-case basis at the final data review meeting.

NOTES:

- The patient must have a documented inadequate or no response, loss of response or an intolerance to at least one of the following:
  - Immunosuppressant treatment (azathioprine, 6-mercaptopurine, methotrexate)
  - TNF inhibitors
  - Vedolizumab
  - JAK inhibitors
  - Corticosteroid treatment.
- Inadequate response, no response, loss of response is defined as:
  - Active disease or relapse despite thiopurines or methotrexate given at an appropriate dose for at least 3 months (i.e. azathioprine 2–2.5 mg/kg/day or mercaptopurine 1–1.5 mg/kg/day in the absence of leukopenia), and/or
  - Active disease despite corticosteroids treatment (prednisolone up to 0.75 mg/kg/day) over a period of 4 weeks, and/or
  - Active disease or relapse despite adequate treatment (as defined in the SmPC) with TNF inhibitors or vedolizumab, and/or
  - Active disease or relapse despite adequate treatment with JAK inhibitors over a period of at least 6 weeks.
- This criterion will be tested using the following data:
  - Previous exposure and level of refractoriness to biological drugs, JAK inhibitors or corticosteroids as captured on the Ulcerative Colitis History (UCHX1) eCRF and obtained from raw.PREVEXP1Y and raw.UCREFRACT.
  - Active disease will be assessed by means of Criterion 6 above.
  - Not meeting this criterion will be captured on the IE eCRF and obtained from raw.IE.IEYN, IECAT and IETESTCD.

- Pregnant or breast-feeding patients

CRITERION [10]: Patient Exhibited Positive Pregnancy Test Result
DEVIATION STATUS: Major/No Major Impact, to be decided on a case-by-case basis at the final

data review meeting.

NOTES:
• Pregnancy will be tested with blood pregnancy tests:
  • Pregnancy test results are captured on the Pregnancy Test (PREG) eCRF and obtained from raw.PREG.HCG_LBORRES.
  • Not meeting this criterion will be captured on the IE eCRF and obtained from raw.IE.IEYN, IECAT and IETESTCD.

- Patients with a history of, or currently suffering from prohibited medical conditions as noted at Screening:

CRITERION [11]: Prohibited Previous or Current Medical Conditions
DEVIATION STATUS: Major/No Major Impact, to be decided on a case-by-case basis at the final data review meeting.

NOTES:
• All patients will be reviewed on a case-by-case basis by the Medical Advisor. A decision will be made on the effect of the potential reason for exclusion to determine if it is considered MAJOR/MINOR.
• The PD related to prohibited medical conditions as identified during the clinical conduct of the study and as authorized in the final PD log will also be considered in this decision.
• Only the data on the Medical History (MH) and Procedure History (PR) eCRF will be sent to the Medical Advisor to flag the cases that are prohibited.
• Previous or current medical conditions in the exclusion criteria include (for details see Section 4.2.2 in the protocol):
  • Crohn's Disease or presence or history of fistula, indeterminate colitis, infectious/ischemic colitis or microscopic colitis.
  • Toxic megacolon, abdominal abscess, symptomatic colonic stricture or stoma, colonic malignancy or history or imminent colectomy.
  • Colonic dysplasia, adenomatous colonic polyps or severe gastrointestinal complications.

- More than one episode of herpes zoster or history (single episode) of disseminated zoster.
- Active infections such as infected abdominal abscess, Clostridium difficile (stool antigen and toxin required), cytomegalovirus (CMV) (positive immunoglobulin M (IgM)), Tuberculosis (TB) and recent infectious hospitalization.
- Acute, chronic or history of clinically relevant pulmonary, cardiovascular, hepatic, pancreatic or renal functional abnormality, encephalopathy, neuropathy or unstable central nervous system (CNS) pathology such as seizure disorder, angina or cardiac arrhythmias, active malignancy or any other clinically significant medical problems as determined by physical examination and/or laboratory screening tests and/or medical history.
- Surveillance colonoscopy not defined as per European Crohn's and Colitis Organization (ECCO) guidelines.
- Acute, chronic or history of immunodeficiency or autoimmune disease.
- History of malignancy excluding patients considered cured (5 years disease free survivors).
- Previous treatment with tube feeding, defined formula diets or parenteral alimentation/nutrition within 3 weeks before the screening visit.
- Serious illness requiring systemic treatment and/or hospitalization within 3 weeks prior to baseline.

- This criterion will be tested using the following data:
  - Medical history is captured on the MH eCRF and obtained from raw.MH.MHTERM, MHSTDAT, MHENDAT and MHONGO. It will be coded as described in Section 11.
  - Procedure history is captured on the PR eCRF and obtained from raw.PR.PRTRT and PRSTDAT.
  - Not meeting these criteria will be captured on the IE eCRF and obtained from raw.IE.IEYN, raw.IE.IECAT and raw.IE.IETESTCD.

- Patients taking prohibited prior and concomitant medications:

CRITERION [12]: Use of Prohibited Medication
DEVIATION STATUS: Major/No Major Impact to be decided on a case-by-case basis at the final BDR meeting.

NOTES:
• All patients will be reviewed on a case-by-case basis by the Medical Advisor. A decision will be made on the effect of the potential reason for exclusion to determine if it is considered MAJOR/NO MAJOR IMPACT.
• The PD related to prohibited prior and concomitant medication use as identified up to Week 8 and as authorized in the final PD log, will also be taken into consideration in the decision.
• The patient may not have taken the following drugs or received the following treatment within the specified period:
  • Topical corticosteroids and topical 5-aminosalicylic acid preparations within 2 weeks prior to Screening.
  • TNF inhibitors, vedolizumab or other biologics within 8 weeks prior to the screening visit
  • Previous treatment with cyclosporine, tacrolimus or JAK inhibitors at least 4 weeks prior to the screening visit
  • Use of any investigational or non-registered product within 3 months or within 5 half-lives preceding baseline, whichever is longer, and during the study.
  • Illicit drug or alcohol use or dependence.
  • Vaccination with live components 30 days or fewer before first dose of study treatment and/or is planning to receive such vaccine during the study duration and upto 8 weeks after last dosing
  • Drugs that inhibit or induce CYP1A2 or inhibt UGTIA9 activity and inhibitors of OATP1B1/1B3 transporters
  • Previous treatment with ABX464.
• This criterion will be tested using the following data:
  • Use of concomitant and prior medication is captured on the Concomitant Medication

(CM) eCRF and obtained from raw.CM.CMTRT, CMSTDAT, CMENDAT, CMONGO and CMPRIOR. It will be coded as described in Section 12. Only the data on the CM eCRF will be sent to the MA to flag the cases that are prohibited. • Not meeting this criterion will be captured on the IE eCRF and obtained from raw.IE.IEYN, IECAT and IETESTCD.

- Patients with unstable dose of permitted concomitant medications within the specified period prior to screening:

CRITERION [13]: Unstable Dose of Permitted Concomitant Medications
DEVIATION STATUS: Major/No Major Impact to be decided on a case-by-case basis at the final DR meeting.

NOTES:
• All patients will be reviewed on a case-by-case basis by the Medical Advisor. A decision will be made on the effect of the potential reason for exclusion to determine if it is considered MAJOR/NO MAJOR IMPACT.
• The PD related to unstable doses of permitted concomitant medication use as identified during the clinical conduct of the study and as authorized in the final PD log, will also be taken into consideration in the decision.
• Permitted concomitant medications must be a stable dose for the specified period prior to screening or baseline:
  • Oral corticosteroids - prednisone or prednisone equivalent (≤20 mg/day) or on beclomethasone dipropionate (≤5mg/day) or on budesonide MMX (≤9mg/day) for at least 2 Weeks prior to the screening visit.
  • Oral 5-aminosalicylic acid for at least 4 weeks prior to screening
  • Immunosuppressants in the form of azathioprine, 6-mercaptopurine, or methotrexate for at least 4 weeks prior to screening visit.
  • Probiotics (e.g. Culturelle® [Lactobacillus GG, i-Health, Inc.], Saccharomyces

boulardii for at least 2 weeks prior to the screening visit.

- Antidiarrheals (e.g., loperamide, diphenoxylate with atropine) for at least 2 weeks prior to the screening visit

- This criterion will be tested using the following data:
  - Use of concomitant and prior medication is captured on the Concomitant Medication (CM) eCRF and obtained from raw.CM.CMTRT, CMSTDAT, CMENDAT, CMONGO and CMPRIOR. Not meeting this criterion will be captured on the IE eCRF and obtained from raw.IE.IEYN, IECAT and IETESTCD.

- Patients who didn't adhere to the visit schedule:

CRITERION [14]: Non-Adherence to the Visit Schedule

DEVIATION STATUS: Major Impact for Baseline and Week 8 visits (primary efficacy end point). No Major Impact for other visits. To be confirmed at the final BDR meeting.

NOTES:

- The table below is guidance provided in the Schedule of Activities in the protocol:

	Study day		
Visit	**Target**	**Lower limit**	**Upper limit**
Screening	n/a	n/a	-31
Day 1 (Baseline)	1	n/a	n/a
Day 8	8	6	10
Day 29	29	27	31
Day 57	57	53	61
Day 85	85	81	89
Day 113	113	109	117
Day 120 (EOS)	120	118	122

For details on the calculation of the study day, see Section 6.1. EOS visit only applies to all premature discontinued patients and patients not taking part in maintenance study. In case of early discontinuation, the patient will be encouraged to return to the study center for the End of Study (EOS) visit within a week after last dosing.

- This criterion will be tested using:
  - The name and date of visit as captured on the Date of Visit (DOV) eCRF and obtained from raw.DOV.VISDAT.
  - The visit for the patient will be flagged only if the day of the actual visit is outside the lower or upper limit. It will be discussed during the BDR meeting whether only the Week 8 and Week 16 visit non-adherence should be regarded as a major deviation.

- Overall study treatment non-compliance (< 80%) up to Week 8:

CRITERION [15]: Treatment Non-Compliance
DEVIATION STATUS: Major/No Major Impact to be decided on a case-by-case basis at the final data review meeting.

NOTES:
• Treatment compliance will be handled as described in Section 14. A patient's compliance will be assessed by considering the number of capsules issued and returned at each visit, as well as the actual number of capsules taken as recorded in the e-diary by the patient.
• This criterion will be tested as follows:
  • Number of capsules dispensed and returned as captured on the DA eCRF and obtained from raw.DA.DAORRES4 and DAORRES5.
  • Number of capsules taken as recorded in the e-diaries.

5.3. DETAILED DATA REVIEW TIMEFRAME

Table E Detailed Timeframe for BDR indicates estimated timings for the data review activities, as well as the person(s) responsible for each activity ("Owner").

Table E Detailed Timeframe for BDR Process

No.	Activity	Owner	Relative Timeframe
1	Data transfer of the clean database to STL (with minimal list of open queries if agreed with STL).	DTL	At least 1 week prior to final data review

			meeting.
2	Provide the data handling report to STL.	DTL	1-2 weeks prior to final data review meeting.
3	Check that the coding has been approved by Abivax and that the reconciliation of the non-eCRF data and of the SAEs has been performed and documented.	DTL	
4	Collect any further necessary input from CPM/PL and DTL.	STL	
5	Preparation and distribution of the draft DR report and other statistics deliverables to CRT.	STL	At least 2 business days prior to final data review meeting.
7	Review all deliverables and the draft DR report.	CRT	
8	Facilitate the data review meeting.	STL	Not applicable
9	Preparation of final data review report.	STL	3 to 4 business days following final data review meeting, prior to DBL.
10	Approval of final data review report.	Abivax	
11	Distribution of the signed data review report in PDF format to CRT.	STL	

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 day of the first dose of study medication. (Day 1 is the day of the first dose of study medication).

- If the date of the event is on or after the reference date, then:

  Study Day = (date of event – reference date) + 1

- If the date of the event is prior to the reference date, then:

  Study Day = (date of event – reference date).

In the situation where 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 taken prior to reference start date (including unscheduled assessments). In the case where the last non-missing measurement and the reference start date coincide, that measurement will be considered pre-baseline, but Adverse Events (AEs) and concomitant medications commencing on the reference start date will be considered post-baseline.

6.3. RETESTS, UNSCHEDULED VISITS AND EARLY TERMINATION DATA

In general, for by-visit summaries, data recorded at the nominal visit will be presented. Unscheduled measurements will not be included in by-visit summaries but will contribute to the best/worst case value where required (e.g. shift table).

In the case of a retest (same visit number assigned), the last available measurement for that visit will be used for by-visit summaries.

Early discontinuation data will be mapped to the next available visit number for by-visit summaries. Listings will include scheduled, unscheduled, retest and early discontinuation data.

6.4. WINDOWING CONVENTIONS

There will be no visit windowing applied in this study.

6.5. STATISTICAL TESTS

The default significant level will be 5%; confidence intervals (CI) will be 95% and all tests will be two-sided, unless otherwise specified in the description of the analyses.

6.6. COMMON CALCULATIONS

For quantitative measurements, change from baseline will be calculated as:

- Test Value at Visit X – Baseline Value

A patient will be considered to have a reduction relative to baseline in variable X at Visit X when change from baseline for variable X is less than zero.

6.7. SOFTWARE VERSION

All derivations, statistical analyses, summaries, and listings will be generated using SAS® version 9.2 or higher (SAS® Institute, Inc., Cary, North Carolina). Graphics will be prepared using the same versions of SAS®.

7. STATISTICAL CONSIDERATIONS

Summaries will include descriptive statistics for continuous variables (sample size [n], mean, standard deviation [SD], median, minimum and maximum) and for categorical variables (frequency [n] and percentage), unless otherwise stated in the relevant section. Percentages will be based on the number of

subjects within the relevant analysis set and treatment arm, or the number of subjects with data available where relevant.

If the original data has N decimal places, then the summary statistics will have the following decimal places:

Minimum and maximum: N

Mean, median, confidence intervals, ratios: N + 1

SD: N + 2

Percentages will be reported to one decimal place. P-values should be reported to three decimal places, except values <1.000 but >0.999 will be presented as '>0.999' (e.g., 0.9998 is presented as >0.999); and values <0.001 will be presented as '<0.001' (e.g., 0.0009 is presented as <0.001)

7.1. ADJUSTMENTS FOR COVARIATES AND FACTORS TO BE INCLUDED IN ANALYSES

The following covariates and factors will be used in the analyses. For details of their inclusion in the models, see the specific analysis section.

Covariates

- Baseline MMS
- Baseline pMMS
- Baseline Fecal Calprotectin level
- Baseline Geboes Score
- Baseline Nancy Score
- Baseline RHI

Factors

- Treatment arm (ABX464 100mg, ABX464 50 mg, ABX464 25mg, Placebo)

- Previous biologic or JAK inhibitors treatment use (Yes/No)

7.2. MULTICENTER STUDIES

This study will be conducted by multiple investigators at multiple centers internationally. Randomization to treatment arms is stratified by previous exposure/non-exposure to biologics and JAK inhibitors treatment use and US/non-US sites.

7.3. MISSING DATA

A subject's missing efficacy data viz. MMS (or any components of MMS missing) at Week 8, will be imputed and the subject will be considered as a non-responder for clinical remission and response.

Missing MMS components at Week 8 will be imputed as follows:
Stool Frequency Sub score: The average of the 3 recent eDiary stool frequency records (if no prior records then choose records after the Week 8 visit date) within 10 days of date of week 8 visit is calculated. The normal stool frequency (at screening) is subtracted from the average and rounded to a whole number. The imputed sub score will be assigned as follows:.
Sub score=0; if calculated value =0
Sub score=1; if calculated value=1,2
Sub score=2; if calculated value=3,4
Sub score=3; if calculated value=5 or greater
If no records available within 10 days from eDairy, the nearest neighbour method will be considered.

Rectal Bleeding Sub score: The worst of the 3 recent eDiary records within 10 days of Date of Week 8 visit, will be considered as the analysis value (if no prior records then choose records after the Week 8 visit date) . If no records available within 10 days from eDairy, the nearest neighbour method will be

considered.

Mucosal appearance at Endoscopy: The analysis value of the nearest neighbour is used to impute missing Endoscopy sub score. The nearest neighbour is defined as the subject in Placebo arm with non-missing sub score, matching the 'subject with missing value' by Gender, Baseline MMS, Age and Previous Exposure to other biologics/JAK status. The matching score is calculated for all the placebo subjects with non-missing sub score, as follows:

1) If the subject matches in gender, 5 points assigned.
2) If previous exposure status matches, then additional 5 points.
3) The absolute difference between the Baseline MMS and Age, is subtracted from the scores.

The Placebo subject with the highest score is considered the nearest neighbour. In case of tied nearest neighbour scores, the worst sub score value will be used to impute.

The imputed components will be used to derive the pMMS (Stool Frequency Sub score + Rectal Bleeding Sub score) and MMS (Stool Frequency Sub score + Rectal Bleeding Sub score + Endoscopy Sub score) at Week 8.

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Missing safety data will not be imputed. Percentages based on the number of subjects with data available will not take missing observations into account.

7.4. MULTIPLE COMPARISONS/ MULTIPLICITY

No adjustment for multiple comparisons is needed, as closed procedures will be applied in testing each dose level vs placebo. The dose testing will commence with comparing the ABX464 50mg dose with placebo. If this is significant at a 5% two-sided level (i.e. $p<0.05$) a comparison against placebo will be carried out at the ABX464 100mg dose. Again, if significance at a 5% level for this test is observed the procedure will be repeated at the ABX464 25mg dose. If in this sequence of comparisons of ABX464 dose levels to placebo, one is not significant (i.e., $p >= 0.05$) the additional comparisons to placebo will not be performed. Should any of the comparisons against placebo be significant, the different dose groups will also be compared, using the same significance level.

7.5. EXAMINATION OF SUBGROUPS

Subgroup analyses will be conducted as described in relevant efficacy analysis sections. It should be noted that the study was not designed to detect treatment differences with high statistical power within subgroups.

Analyses will be performed for the following subgroups:

- Gender:
  - Female
  - Male
- Age (years):
  - <30
  - ≥30 to <65
  - ≥65
- Country/Region

Austria	Netherlands
Belarus	Poland
Belgium	Serbia
Canada	Slovakia
Czech Republic	Slovenia
France	Spain
Germany	Ukraine
Hungary	United Kingdom
Italy	US

North America (US and Canada).

Western Europe: Italy, France, Germany, Netherlands, Austria, Belgium, Spain, United Kingdom

Eastern Europe: Slovakia, Slovenia, Ukraine, Poland, Czech Republic, Serbia, Hungary, Belarus

- Baseline MMS:

4

5 to 6

7 to 9

- With/without previous biological or JAK inhibitors exposure
- Concomitant UC medications

  Corticosteroids

  Immunosuppressants

  5ASA

8. OUTPUT PRESENTATIONS

APPENDIX 1 shows conventions for presentation of data in outputs. The templates provided with this SAP describe the presentations for this study and therefore the format and content of the summary tables, figures, and listings to be provided by IQVIA Biostatistics.

9. DISPOSITION AND WITHDRAWALS

All patients who provide informed consent will be accounted for in this study. The number and the percentages of patients enrolled and included in each of the analysis sets, as well as reasons for exclusion from each of the analysis sets, will be tabulated. In addition, the number of screen and baseline failures, as well as discontinued patients with their reason for treatment discontinuation will be tabulated. Protocol deviations will be reviewed and classed as critical, major or minor during the BDR meeting and listed as such.

Listings will include assigned treatment, completion or early discontinuation, and the reason for early discontinuation for each patient, as well as details of protocol deviations, screen and baseline failures and inclusion/exclusion criteria not met, analysis sets and enrolment in the maintenance study (ABX464-104). A cumulative incidence plot of time to discontinuation by study treatment will also be provided.

10. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographic data and other baseline characteristics will be presented for the FAS and PPAS and summarized by treatment arm. No statistical testing will be carried out for demographic or other baseline characteristics.

The following demographic and other baseline characteristics will be reported for this study:

- Age (years)
- Gender
- Country/Region
- Weight (kg)
- Height (cm)
- Body Mass Index (kg/m^2)
- Tobacco usage (number of packs per year)
- Baseline MMS
- With/without previous biological or JAK inhibitors exposure (Refractoriness)
- Concomitant UC medication
- UC history (Time since diagnosis of ulcerative colitis (years), Disease Extent)

10.1. DERIVATIONS

10.1.1. BODY MASS INDEX (BMI)

- Body Mass Index (BMI) (kg/ m^2) = weight (kg)/height (m)^2

10.1.2. TIME SINCE STOPPING TOBACCO USAGE (FORMER SMOKERS)

Time since stopping tobacco usage is determined from date of stopping to date of IC.

If the full date of tobacco stop date is available, then:

- Time since stopping tobacco usage (years) = (Date of IC – Tobacco stop date + 1)/365.25

If only the year and month of tobacco stop date are available, the date will be imputed using first day of the month.

If only the year of tobacco stop date is available, the day and month from the IC date will be used to impute the tobacco stop date.

10.1.3. NUMBER OF PACKS PER YEAR

For Current and Former smokers, number of packs is determined as follows:

- If Frequency = Per day, then Number of packs/year = Amount as indicated * 365.25.
- If Frequency = Per week, then Number of packs/year = (Amount as indicated / 7) * 365.25
- If Frequency = Occasional, Number of packs used occasionally = Amount as indicated.

10.1.4. TIME SINCE DIAGNOSIS OF ULCERATIVE COLITIS

Duration of the disease will be calculated from the date of disease onset to the date of IC.

If the full date of disease onset is available, then:

- Time since diagnosis (years) until IC = (Date of IC – Date of onset of ulcerative colitis +1) / 365.25

If only the year and month of date of disease onset are available, the date will be imputed using first day of the month.
If only the year of date of disease onset is available, the day and month from the IC date will be used to impute the onset date.

11. SURGICAL AND MEDICAL HISTORY

The medical history information including procedures will be listed for the SAF analysis set. Conditions or procedures which stop prior to or at screening will be recorded Any other medical condition or procedure occurring after screening will be recorded as an adverse event.

Medical History will be coded using the latest version of the Medical Dictionary for Regulatory Activities (MedDRA) (currently version 23.0). Data captured on the Medical and Procedure History pages of the eCRF will be listed by patient and Medical History will include System Organ Class (SOC) and Preferred Term (PT) coding.

12. PRIOR AND CONCOMITANT MEDICATIONS

Concomitant medications will be summarized and listed for the SAF and coded using the latest version of the World Health Organization Drug Dictionary (WHODD) Global version (currently WHODD Global March 2019 B3) and Anatomical Therapeutic Chemical (ATC) system. Prior and concomitant medications will be listed.

- 'Prior' medications are medications which started and stopped prior to the first dose of study medication.
- 'Concomitant' medications are medications which started prior to, on or after the first dose of study medication, but on or before the last dose of study medication, and ended on or after the date of first dose of study medication or were ongoing at the end of the study.

See APPENDIX 3 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.

13. STUDY MEDICATION EXPOSURE

Exposure to study medication in days will be summarized for the FAS and PPAS.

The dates of first study medication administration and last study medication administration will be obtained from the eCRF Exposure form (EC). In the case of missing data on the eCRF, the diary data will be used to determine the first and last date of study medication. Interruptions and compliance are not considered for duration of exposure.

13.1. DERIVATIONS

- Overall duration of study treatment exposure (days) = End dose date of last study medication administration – Start dose date of first study medication administration + 1.

14. STUDY MEDICATION COMPLIANCE

Compliance to study medication will be presented for the FAS and PPAS.

Compliance with double-blind study medication will be calculated as the number of capsules taken (total dispensed – total returned and confirmed by e-diary entries) divided by the expected number of capsules expressed as a percentage.

Patients will take 2 capsules per day, from Day 1 to Day 112, regardless of treatment group. They will receive 70 capsules at each dosing visit (Days 1, 29, 57 and 85) and compliance for these visits will be determined by the number of capsules returned at the next visit (Days 29, 57, 85 and 113). The number of capsules dispensed and returned will be obtained from the Drug Accountability eCRF page and e-Diaries completed by patients. For patients who permanently stop the study medication, the last visit will be replaced by the date of study withdrawal.

14.1. DERIVATIONS

- Compliance up to Week 8 will be calculated using:

$$\frac{\text{No.Capsules dispensed at Day 1} - \text{No.Capsules returned at Day 57}}{\text{Total expected number of capsules for the period (2 per day)}} \times 100$$

- Overall Compliance to study medication will be calculated as follows:

$$\frac{\text{Total number of Capsules taken from Day 1 to Day 112}}{\text{Total expected number of capsules for the period (2 per day)}} \times 100$$

15. EFFICACY OUTCOMES

15.1. PRIMARY EFFICACY

15.1.1. PRIMARY EFFICACY VARIABLE & DERIVATION

The primary efficacy variable is the reduction from baseline in MMS at Week 8 (Day 57).

The MMS will be obtained from the MMS eCRF page with raw.MMS.MMSSCR and confirmed by eDiary entries. The MMS ranges from 0 to 9 and is derived from the sum of 3 sub-scores ranging from 0 to 3 for stool frequency, rectal bleeding and mucosal appearance at endoscopy respectively, with a lower score indicating less severe or no ulcerative colitis (UC) (See APPENDIX 2). The MMS determined at screening will be used as baseline MMS, as MMS is not calculated at Day 1.

Change from baseline is described in Section 6.6.

15.1.2. Missing Data Methods for Primary Efficacy Variable

Subjects with missing primary efficacy values will be imputed as non-responders for clinical remission and response at Week 8. Missing MMS scores at Week 8 will be imputed as mentioned in section 7.3.

15.1.3. Primary Analysis of Primary Efficacy Variable

The primary efficacy analysis will be performed for FAS and PPAS.

The primary objective of this study is to determine an optimal ABX464 dose to be used in moderate to severe active ulcerative colitis patients who have failed or are intolerant to immunomodulators, Anti-TNFα, vedolizumab, JAK inhibitors and/or corticosteroids by comparing the mean change from baseline in the MMS at Week 8 for the three ABX464 dose levels to the placebo. An analysis of covariance (ANCOVA) model will be used to assess these changes.

The ANCOVA model for Change from Baseline MMS at Week 8 will include the fixed treatment effect, the previous use of biological or JAK inhibitors effect and the covariate, baseline MMS and a random error term.

The assumptions that the random errors in the ANCOVA model are normally distributed with homogeneity of variances will be checked. If either the hypothesis regarding normality of errors or the hypothesis of equal variances is rejected at the 5% significance level a nonparametric ANCOVA using the ranked data will be performed to test for differences in the mean change from baseline. The least square means and confidence intervals from the parametric ANCOVA will also be presented.

The dose testing will commence with comparing the ABX464 50mg dose with placebo. If this is significant at a 5% two-sided level (i.e. $p<0.05$) a comparison against placebo will be carried out at the ABX464 100mg dose. Again, if significance at a 5% level for this test is observed the procedure will be repeated at the ABX464 25mg dose. If in this sequence of comparisons of ABX464 dose levels to placebo one is not significant (i.e., $p >= 0.05$) the additional comparisons to placebo will not be

performed. Should any of these comparisons with the placebo treatment group be significant, further exploratory testing of the dose groups against each other will be conducted at the same significance level. A global comparison of all active treatment groups vs placebo group will also be conducted.

Descriptive statistics for MMS and change from baseline MMS at every visit assessed will be summarized by treatment arm in a table and displayed graphically. A by subject listing of the MMS values and change from baseline value will also be presented.

15.1.4. Sensitivity Analysis of Primary Efficacy Variable

15.1.4.1. Per Protocol Analyses

The primary efficacy analysis will be repeated for the PPAS. Similar output will be displayed for these results.

15.1.4.2. Subgroup Analyses

The primary efficacy analysis will be repeated for the subgroups Age, Gender, concomitant UC medications, with/without previous biological or JAK inhibitors exposure and Baseline MMS, as explained in Section 7.5.

15.2. Secondary Efficacy

The secondary efficacy analyses will be performed for the FAS and PPAS. Descriptive statistics will be presented by treatment arm for all secondary efficacy variables for each measurement timepoint, including mean, SD, minimum, maximum, median, quartiles and 95% CI for the mean for continuous variables. Number and percentage of subjects and the 95% CI for the percentage will be calculated for categorical variables. Descriptive statistics for change from baseline will also be determined where

relevant and is defined in Section 6.6.

15.2.1. SECONDARY EFFICACY VARIABLES & DERIVATIONS

15.2.1.1. Number and Percentage of Patients in Clinical Remission at Week 8 and Week 16

Clinical remission is defined as:

- A stool frequency subscore = 0 or 1
- A rectal bleeding sub-score = 0
- An endoscopy sub-score = 0 or 1 (modified to exclude friability)

This endpoint will be calculated per treatment arm and presented descriptively.

$$\text{Percentage of patients in clinical remission at Week 8} = \frac{\text{Number of patients in treatment arm with clinical remission at Week 8}}{\text{Total number of patients in the treatment arm}} \text{ x } 100$$

$$\text{Percentageof patients in clinical remission at Week 16} = \frac{\text{Number of patients in treatment arm with clinical remission at Week 16}}{\text{Total number of patients in the treatment arm at Week 16}} \text{ x } 100$$

$$\text{Percentage of patients in clinical remission at Week 8 or Week 16} = \frac{\text{Number of patients in treatment arm with clinical remission at Week 8 or Week 16}}{\text{Total number of patients in the treatment arm at Week 8 or Week 16}} \text{ x } 100$$

Number of patients with clinical remission at week8 and not at week 16 as well as number of patients with clinical Remission at Week 16 and not at Week 8 will also be presented.

15.2.1.2. Combined Number and Percentage of Patients in Clinical Remission at Week 8 and Week 16

Clinical remission is defined in Section 15.2.1.1. The number and percentage of patients in clinical remission at both Week 8 and Week 16 will be summarized by treatment arm.

$$\text{Percentage of patients in clinical remission at Week 8 and Week 16} = \frac{\text{Number of patients in treatment arm with clinical remission at Week 8 and Week 16}}{\text{Total number of patients in the treatment arm at both visits}} \text{ x } 100$$

15.2.1.3. Number and Percentage of Patients with Clinical Response at Week 8 and Week 16

Clinical response is defined as

- A reduction from baseline in MMS $\geq$ 2 points, and
- A reduction in MMS $\geq$ 30% from baseline with a decrease in rectal bleeding sub-score $\geq$ 1 point or absolute rectal bleeding sub-score $\leq$ 1 point

This endpoint will be summarized by treatment arm.

$$\text{Percentage of patients with clinical response at Week 8 and Week 16} = \frac{\text{Number of patients in treatment arm with clinical remission at Week 8 and Week 16}}{\text{Total number of patients in the treatment arm}} \text{ x } 100$$

Number of patients with clinical response at week8 and not at week 16 as well as number of patients with clinical response at Week 16 and not at Week 8 will also be presented.

15.2.1.4. Number and Percentage of Patients with Endoscopic Improvement and Remission, by Segment at Week 8 and Week 16

Endoscopic improvement is defined as an endoscopic sub-score ≤ 1 and endoscopic remission is defined as an endoscopic sub-score = 0. The improvement and remission will be summarized by segment (descending colon, sigmoid colon, rectum) as well as overall endoscopic improvement and remission for Week 8 and Week 16.

$$\text{Percentage of patients with endoscopic improvement (or remission) at Week 8 for segment X} = \frac{\text{Number of patients in treatment arm with endoscopic improvement (or remission) at Week 8 in segment X}}{\text{Total number of patients in the treatment arm for segment X at Week 8}} \text{ x } 100$$

The percentage of patients with endoscopic improvement or remission at Week 16 for segment X will be calculated similarly for data available at Week 16.

The overall percentage of patients with endoscopic improvement or remission at Week 8 will be calculated as follows:

$$\text{Percentage of patients with endoscopic improvement (or remission)at Week 8} = \frac{\text{Number of patients in treatment arm with endoscopic improvement (or remission) at Week 8}}{\text{Total number of patients in the treatment arm at Week 8}} \text{ x } 100$$

The overall percentage of patients with endoscopic improvement or remission at Week 16 will be calculated similarly for data available at Week 16.

Number of patients with endoscopic improvement and endoscopic remission, by segment at week8 and not at week 16 as well as number of patients with endoscopic improvement and endoscopic remission, by segment at Week 16 and not at Week 8 will also be presented.

15.2.1.5. Number and Percentage of Patients with Mucosal Healing at Week 8 and Week 16

Mucosal healing is defined as both endoscopic remission and histological remission (Geboes score < 2.0)

A patient is said to be in Histological Remission, if severity of Geboes score component (APPENDIX 4) grades (2A, 2B, 3, 4 & 5) are zero with non-missing grades (0 and 1).

Numerical Geboes Score is the sum of all the components (Grades: 0-Architectural changes, 1-Chronic inflammatory infiltrate, 2A-Eosinophils in lamina propria, 2B- Neutrophils in lamina propria, 3-Neutrophils in epithelium, 4-Crypt destruction and 5-Erosions and ulcerations).

Descriptive Statistics and MMRM are based on Numerical Geboes score. Geboes score is based on rectal biopsy only.

$$\text{Percentage of patients with mucosal healing at Week 8 (or Week 16)} = \frac{\text{Number of patients in treatment arm with mucosal healing at Week 8 (or Week 16)}}{\text{Total number of patients in the treatment arm at Week 8 (or Week 16)}} \text{ x } 100$$

Number of patients with mucosal healing at week8 and not at week 16 as well as number of patients with mucosal healing at Week 16 and not at Week 8 will also be presented.

15.2.1.6. Reduction Relative to Baseline in Stool Frequency and Rectal Bleeding

Number and percentage of patients in each Mayo stool frequency category will be summarized at every study visit and the number of patients with reduction in stool frequency sub-score relative to baseline will be recorded. The stool frequency sub-score corresponds to the **average** of the 3 most recent daily stool frequencies prior to the visit, rounded to the nearest whole number. The normal stool frequency is subtracted from this average to obtain the Mayo stool frequency sub-score for a particular visit. Frequency of stools will be obtained from e-Diaries completed daily by the patient.

Descriptive statistics for stool frequency sub-score and its change from baseline will be presented by visit.

The frequency sub-score will be calculated as described above. Reduction relative to baseline is defined in Section 6.6.

Number and percentage of patients in each rectal bleeding category will be summarized. The number of patients indicating an improvement in rectal bleeding sub-score from the baseline rectal bleeding sub-score will be recorded. The rectal bleeding sub-score corresponds to the **worst category** of the 3 most recent values prior to the visit.

Only days when both the number of stool and the rectal bleeding are available will be considered for the calculation. If some data are missing from the most recent consecutive 3 days preceding the visit, then data from the next closest days within 7 days before the visit will be used for calculation.

15.2.1.7. Reduction Relative to Baseline in pMMS at every Visit and MMS at Week 16

Partial MMS will be assessed at every visit, and MMS at Screening, Week 8 and Week 16. Partial MMS is the sum of the stool frequency and rectal bleeding sub-scores of the MMS.

The screening MMS will be used as baseline MMS. Day 1 pMMS will be used as baseline pMMS. Absolute scores and change from baseline will be summarized by treatment arm, and the number of patients with a reduction relative to baseline in the scores will be recorded. Reduction relative to baseline is defined in Section 6.6

15.2.1.8. Global Effect of ABX464 Treatment vs Placebo in Change from Baseline in MMS at Week 8 and Week 16 and in pMMS at every study visit

The global effect of ABX464 treatment will be assessed by comparing the MMS scores at Week 8 and Week 16 and pMMS scores at every visit of the active treatment groups combined vs placebo group.

15.2.1.9. Reduction relative to Baseline in Fecal Calprotectin and CRP Levels at Week 8 and Week 16

Change from baseline in Fecal Calprotectin and CRP levels will be determined at Week 8 and Week 16. The number of patients with a reduction relative to baseline in Fecal Calprotectin and CRP levels will also be recorded. Reduction relative to baseline is defined in Section 6.6.

15.2.1.10. The Inflammatory Bowel Disease Questionnaire Scores and Change from Baseline at Week 8 and Week 16

The IBDQ is used to asses QoL in patients with inflammatory bowel diseases (IBD). It contains 32 questions covering four health domains (bowel symptoms, systemic symptoms, emotional function and social function) and scores for each question range from 1 (worst case) to 7 (best case). The total IBDQ score ranges from 32 to 224, with higher scores reflecting better well-being. The total scores and change from baseline will be determined at Week 8 and Week 16 and summarized by treatment arm.

15.2.1.11. Reduction relative to baseline of infiltrate/histopathology (rectal biopsies) using the Robarts Histopathology Index (RHI), the Geboes and Nancy Histology Scoring Scales at Week 8 and Week 16

Change from baseline in RHI, Geboes and Nancy scores will be determined at Week 8 and Week 16. The number of patients with a reduction relative to baseline in RHI, Geboes and Nancy scores will also be recorded. Reduction relative to baseline is defined in Section 6.6.

15.2.2. Missing Data Methods for Secondary Efficacy Variable(s)

E-diary entries will be used to estimate missing stool frequency and rectal bleeding scores as these values are recorded daily in the e-diary. Endoscopy sub score missing data methods are also specified in section 7.3

15.2.3. ANALYSIS OF SECONDARY EFFICACY VARIABLES

15.2.3.1. Analysis of Secondary Variables at Week 8 and at Week 16

In addition to the descriptive statistics as described in Section 15.2 and specific subsections of Section 15.2. ANCOVA models, using the same procedure as described for the primary efficacy analysis in section 15.1.3, will be used to make the assessments listed below:

- Global effect of ABX464 treatment vs placebo in change from baseline in MMS at Week 8
- Combined number and percentage of patients in clinical remission at Week 8 and Week 16
- The number and percentage of patients with clinical response at Week 8 and Week 16
- The number and percentage of patients with endoscopic improvement and remission, by segment at Week 8 and Week 16
- Proportion of patients with mucosal healing at Week 8 and Week 16
- Daily stool frequency and number of patients with reduction relative to baseline in stool frequency sub-score at every study visit
- Number of patients with reduction relative to baseline in rectal bleeding sub-score at each visit
- Frequencies and percentages for rectal bleeding and stool frequency sub-score categories
- Frequencies and percentages for Mucosal Appearance at endoscopy by segment
- Total IBDQ scores and change from baseline at Week 8 and Week 16

In addition, the above variables will be included in a listing by patient. The frequency of daily stools and categories of rectal bleeding as recorded in the e-Diary will be listed for the duration of the study.

[redacted]

15.2.3.2. Analysis of Number and Percentage of Patients in Clinical Remission at Week 8

The proportion of patients with clinical remission at Week 8 will be compared across study treatment arms using a stratified Mantel-Haenszel test to estimate the common odds ratio for each active arm vs placebo, with exposure to previous biological or JAK inhibitors as the stratification factor. As the common odds ratio is calculated under the assumption that the underlying odds ratio is homogeneous across the strata, the hypothesis of homogeneity of the odds ratio across strata will be tested using the Breslow-Day test. The chi-square, degrees of freedom and corresponding p-value for the Breslow-Day test for homogeneity of the odds ratios will be presented. A p-value less than 5% will indicate that the assumption of a common odds ratio is unreasonable. In this case, the Cochran-Mantel-Haenszel estimate of the common odds ratio will not be reported, but rather the strata-specific (i.e. previous exposure to biological or JAK inhibitors) estimates of the odds ratio.

If a sample size is too small for the hypothesis of homogeneity of the odds ratio to be tested by the Breslow-Day test, the stratum -specific or unstratified odds ratio will be determined.

15.2.3.3. Analysis of Secondary Variables Measured Repeatedly Over Time

In addition to descriptive statistics as described in Section 15.2, mixed model repeated measures ANCOVA will be used to assess the following secondary variables:

- Change from screening in MMS to Week 8 and Week 16 and change from baseline to all post-baseline visits in pMMS during the study, by treatment group vs placebo group.
- The change from baseline in fecal calprotectin levels at Week 8 and Week 16.
- The change from screening in the histopathology/infiltrate (rectal biopsies) assessed by the Robarts Histopathology Index, the Geboes and Nancy Histology Scoring Scales at Week 8 and Week 16 (if available).

Mixed Model for Repeated Measures (MMRM) will be used to analyze change from baseline in MMS, pMMS, fecal calprotectin, RHI, Geboes and Nancy scores. Change from baseline at the specified Week

will be analyzed by using a MMRM model with baseline value as a covariate, fixed effects for treatment group, exposure to previous biologics or JAK inhibitors, visit, visit by treatment group interaction and a random error term. For the MMRM model, the Kenward-Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used. This will be achieved by specifying the DDFM = KR option in the MODEL statement within PROC MIXED. An unstructured covariance will be selected initially, and if convergence is not achieved with this structure, the following covariance structures will be used in the order listed until convergence is achieved: Toeplitz (TOEP), Autoregressive (AR) and Compound Symmetry (CS).

The strata US vs non-US sites will not be included as a factor in the model as the stratification occurs only because US patients will not receive 100 mg dose of ABX464.

16. PHARMACOKINETICS

The analysis of PK concentrations and parameters will be completed by a separate vendor.

17. SAFETY OUTCOMES

All outputs for safety outcomes will be based on the SAF. There will be no statistical comparisons between the treatment groups for safety data, unless otherwise specified in the relevant section.

17.1. ADVERSE EVENTS

Adverse Events will be coded using the latest version of MedDRA, down to the lower level term (LLT).

Treatment emergent adverse events (TEAEs) are defined as AEs that started or worsened in severity on or after the first dose of study medication. As AEs will be recorded up to 4 weeks after study drug treatment has ended, AE will be considered treatment-emergent even if started after the last dose date. Adverse

events occurring after Day 113 will be flagged in the AE listing.

An overall summary of number of patients within each of the categories described in the sub-sections below, as well as the number of occurrences of the AE will be provided as specified in the templates. Listings will include TEAEs and Non-TEAEs.

See APPENDIX 3 for handling of partial dates for AEs. In the case where it is not possible to define an AE as treatment emergent or not, the AE will be classified by the worst case; i.e. treatment emergent.

17.1.1. ALL TEAEs

Incidence of TEAEs will be presented by SOC and PT and also broken down further by maximum severity and relationship to study medication.

17.1.1.1. Severity

Severity is classed as mild, moderate, severe, life-threatening and fatal corresponding to the Common Terminology Criteria of Adverse Events (CTCAE) grades 1 to 5 (increasing severity) (Version 5.0 or most recent version). TEAEs starting after the first dose of study medication with a missing severity will be classified as severe. If a patient reports a TEAE more than once within that SOC/PT, the AE with the worst-case severity will be used in the corresponding severity summaries.

17.1.1.2. Relationship to Study Medication

Relationship, as indicated by the Investigator, is classed as Unrelated, Unlikely to be Related, Possibly Related, Probably Related and Related (increasing severity of relationship). TEAES will be summarized as "Related" or "Unrelated". A "related" TEAE is defined as a TEAE with a relationship to study medication as *"possibly related", "probably related" or "related"* to study medication, and an "unrelated" TEAE is either "*unrelated*" or "*unlikely to be related*" to study medication. TEAEs with a missing relationship to study medication will be regarded as "*probably related"* to study medication. If a

patient reports the same AE more than once within that SOC/ PT, the AE with the worst-case relationship to study medication will be used in the corresponding relationship summaries.

17.1.2. Serious Adverse Events

Serious adverse events (SAEs) are those events recorded as “Serious” on the Adverse Events page of the eCRF. A summary of serious TEAEs by SOC and PT will be prepared, as well as related treatment-emergent SAEs by maximum severity will be prepared. A listing of all SAEs will also be presented.

17.1.3. TEAEs Leading to Discontinuation of Study Medication

TEAEs leading to permanent discontinuation of study medication will be identified by using the response “Permanent discontinuation” to the question “Action taken with study treatment” on the AE page of the eCRF. For TEAEs leading to discontinuation of study medication, summaries of incidence rates (frequencies and percentages) by SOC and PT will be prepared.

17.1.4. TEAEs Leading to Discontinuation from Study

TEAEs causing the patient to discontinue from the study will be identified by a positive response to the question “Did the AE cause the patient to discontinue from the study?” and will be summarized by SOC and PT.

17.1.5. Adverse Events Leading to Death

TEAEs leading to death are those events which are recorded as 'Fatal' on the Adverse Events page of the eCRF. A summary of TEAEs leading to death by SOC and PT will be prepared.

17.1.6. Adverse Events Of Special Interest

Treatment-emergent adverse events of special interest (AESI) associated with treatment with ABX464

include skin lesions and headache episodes lasting longer than a week and refractory to standard painkillers and will be recorded as an AE of interest on the eCRF AE form. A summary of AESIs by SOC and PT will be prepared, as well as a further summary and listing of information on headache episodes, obtained from the Follow up Headache Questionnaire on the eCRF.

17.2. LABORATORY EVALUATIONS

Results from the central laboratory for hematology and biochemistry, including blood pregnancy tests will be included in the reporting of this study. A list of laboratory assessments to be included in the outputs is presented in Table F below.

The results of Fecal Calprotectin levels will not be communicated to the study Sponsor, Investigational Site or blinded biostatistical team during the study to avoid any possible bias related to disease evaluation. These results will be made available post DBL in the unblinded final analyses.

Presentations will use *Systeme International* (SI) Units.

Quantitative laboratory measurements reported as "< X", i.e. below the lower limit of quantification (BLQ), or "> X", i.e. above the upper limit of quantification (ULQ), will be converted to X for quantitative summaries, but will be presented as recorded, i.e. as "< X" or "> X" in the listings.

The following summaries will be provided for laboratory data:

- Actual and change from baseline by visit (for quantitative measurements)
- Shift from baseline according to laboratory approved normal ranges (Low, Normal, High) for quantitative measurements
- Incidence of clinically significant abnormalities
- Listing of patients meeting abnormal criteria

The following clinical laboratory parameters will be summarized using descriptive statistics (n, mean, SD,

standard error of the mean [SEM], median, minimum and maximum.):

Table F Laboratory Tests

HEMATOLOGY	BIOCHEMISTRY	STOOLS
Basophils	Alanine Aminotransferase (SGPT)	Fecal Calprotectin
Basophils/100 Leukocytes	Albumin	
Eosinophils	Alkaline Phosphatase	
Eosinophils/100 Leukocytes	Aspartate Aminotransferase (SGOT)	
Erythrocyte Mean Corpuscular Hemoglobin Concentration	Bilirubin, Total	
Erythrocyte Mean Corpuscular Volume	Blood Urea Nitrogen	
Hematocrit	C Reactive Protein	
Hemoglobin	Calcium	
Lymphocytes	Chloride	
Lymphocytes/100 Leukocytes	Cholesterol, Total	
Monocytes	Creatinine	
Monocytes/100 Leukocytes	Creatinine Clearance (Est)	
Neutrophils	Gamma Glutamyl Transferase	
Neutrophils/100 Leukocytes	Glucose	
Platelets	Glutamate Dehydrogenase	
Red Blood Cells	HDL Cholesterol	
White Blood Cells	LDL Cholesterol	
	Lactate Dehydrogenase	
	Lipase	
	Phosphorus	
	Potassium	
	Protein	
	Sodium	

17.2.1. LABORATORY REFERENCE RANGES AND AGE CRITERIA

Quantitative laboratory measurements will be compared with the relevant laboratory reference ranges in SI units and categorized as:

- Low: Below the lower limit of the laboratory reference range.
- Normal: Within the laboratory reference range (upper and lower limit included).
- High: Above the upper limit of the laboratory reference range.

In addition to the high and low quantitative laboratory assignments (as identified by means of the laboratory reference ranges), abnormalities will be classified as not clinically significant or clinically

significant.

17.3. ECG EVALUATIONS

Overall assessment of the results from the central ECG Reading Center will be included in the reporting of this study and summarized by frequency and percentage of patients in each assessment category for every visit and treatment group.

Overall assessment of ECG (Investigator's judgment) will be reported as follows:

- Normal
- Abnormal NCS
- Abnormal CS

The following summaries will be provided for ECG data:

- Incidence of overall assessments (normal, abnormal NCS, abnormal CS)
- Shift from baseline according to overall assessment of ECG

17.4. VITAL SIGNS

Descriptive statistics including n, mean, SD, SEM, median, minimum and maximum will be summarized for all vital sign parameters.

The following vital sign measurements will be reported for this study:

- Systolic Blood Pressure (SBP) (mmHg)
- Diastolic Blood Pressure (DBP) (mmHg)
- Heart Rate (beats/min)
- Body Temperature (^{0}C)
- Weight (kg)

- Baseline Height (cm)
- BMI (kg/m^2)

The following summaries will be provided for vital signs data:

- Actual and change from baseline by visit
- Incidence of clinically significant abnormal results for each parameter and visit
- Shift table for number of patients with abnormal results
- Listing of results by patient, including abnormal observations

17.4.1. Vital Signs Clinically Significant Criteria

Abnormal vital sign assessments will be reported in accordance with the following predefined abnormal criteria:

Variable	Unit	Low	High
SBP	mmHg	≤ 90 mmHg AND change from baseline ≤ -20 mmHg	≥ 180 mmHg AND change from baseline ≥ 20 mmHg
DBP	mmHg	≤ 50 mmHg AND change from baseline ≤ -15 mmHg	≥ 105 mmHg AND change from baseline ≥ 15 mmHg
Heart rate	Bpm	≤ 50 bpm AND change from baseline ≤ -15 bpm	≥ 120 bpm AND change from baseline ≥ 15 bpm
Body temperature	˚C	NA	≥ 38.3 ˚C AND change from baseline ≥ 1.1 ˚C
Weight	Kg	percentage change from baseline ≤ -7.0 %	percentage change from baseline ≥ 7.0 %

17.5. Physical Examination

The following assessments will be taken at every physical examination: eyes, ears, nose and throat, lungs/thorax, heart/cardiovascular system, abdomen, skin and mucosae, nervous system, lymph nodes and

musculo-skeletal system.

Results will be captured by the following categories:

- Normal
- Abnormal, NCS
- Abnormal, CS

Only abnormal findings will be presented in a listing.

18. REFERENCES

1. A randomized, double blind, placebo controlled, parallel group, multiple dose, induction study to evaluate the safety, tolerability and optimal dose of ABX464 compared with placebo in patients with moderate to severe ulcerative colitis who have inadequate response, loss of response, or intolerance with at least one of the following agents: immunosuppressant treatment (i.e. azathioprine, 6-mercaptopurine, methotrexate), tumor necrosis factor alpha [TNF-α] inhibitors, vedolizumab, JAK inhibitors and/or corticosteroid treatment. Abivax. Protocol ABX464-103 Version 3.0 1 June 2020.

2. Abivax. eCRF ABX464-103 Version 10 19 Feb 2021

APPENDIX 1. PROGRAMMING CONVENTIONS FOR OUTPUTS

IQVIA OUTPUT CONVENTIONS

Outputs will be presented according to the guidelines in the IQVIA Biostatistics Output Conventions.

DATES & TIMES

Depending on data available, dates and times will take the form yyyy-mm-ddThh:mm:ss.

SPELLING FORMAT

English US

PRESENTATION OF TREATMENT GROUPS

For outputs, treatment groups will be represented as follows and in that order:

Treatment Group	For Tables, Listings and Graphs
ABX464 100 mg	100 mg
ABX464 50 mg	50 mg
ABX464 25 mg	25 mg
Placebo	Placebo
Not Treated	Not Treated
Not Randomized	Not Randomized

PRESENTATION OF VISITS

For outputs, visits will be represented as follows and in that order:

Long Name (default)	**Short Name**
Screening	SC
Randomization	Randomization
Baseline (Day 1)	Baseline
Day 8	D8
Day 29	D29
Week 8 (Day 57)	D57
Day 85	D85
Week 16 (Day 113)	D113
EOS (Day 120)	EOS

LISTINGS

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

- Treatment
- Site-Patient ID
- Date (where applicable)
- For listings where not treated or non-randomized patients are included, these will appear in a category after the randomized treatment groups labelled “Not Treated” and “Not Randomized”.

APPENDIX 2. **MAYO SCORE**

Components of the Mayo Score	
Stool frequency	
0	Normal
1	1–2 stools/day more than normal
2	3–4 stools/day more than normal
3	5 or more stools/day more than normal
Rectal bleeding	
0	None
1	Visible blood with stool less than half the time
2	Visible blood with stool half of the time or more
3	Passing blood alone
Mucosal appearance at endoscopy	
0	Normal or inactive disease
1	Mild disease (erythema, decreased vascular pattern, mild friability
2	Moderate disease (marked erythema, absent vascular pattern, friability, erosions)
3	Severe disease (spontaneous bleeding, ulceration)
Physician rating of disease activity	
0	Normal
1	Mild
2	Moderate
3	Severe

APPENDIX 3. PARTIAL DATE CONVENTIONS

Imputed dates will NOT be presented in the listings.

ALGORITHM FOR TREATMENT EMERGENCE OF ADVERSE EVENTS:

START DATE	STOP DATE	ACTION
Known	Known/Partial/Missing	If start date < study med start date, then not TEAE If start date >= study med start date, then TEAE
Partial, but known components show that it cannot be on or after study med start date	Known/Partial/Missing	Not TEAE
Partial, could be on or after study med start date	Known	If stop date < study med start date, then not TEAE If stop date >= study med 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 med start date, then not TEAE If stop date >= study med start date, then

START DATE	STOP DATE	ACTION
		TEAE
	Missing	Assumed TEAE
Missing	Known	If stop date < study med start date, then not TEAE If stop date >= study med 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 med start date, then not TEAE If stop date >= study med start date, then TEAE
	Missing	Assumed TEAE

ALGORITHM FOR PRIOR / CONCOMITANT MEDICATIONS:

START DATE	STOP DATE	ACTION
Known	Known	If stop date < study med start date, assign as prior If stop date >= study med start date and start date <= end of treatment, assign as concomitant

START DATE	STOP DATE	ACTION
	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 med start date, assign as prior If stop date >= study med start date and start date <= end of treatment, assign as concomitant
	Missing	If stop date is missing could never be assumed a prior medication If start date <= end of treatment, assign as concomitant
Partial	Known	Impute start date as earliest possible date (i.e. first day of month if day unknown or 1st January if day and month are unknown), then: If stop date < study med start date, assign as prior If stop date >= study med start date and start date <= end of treatment, assign as concomitant
	Partial	Impute start date as earliest possible date (i.e. first day of month if day 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 or 31st December if day and month are unknown), then: If stop date < study med start date, assign as prior If stop date >= study med start date and start date <= end of treatment, assign as concomitant
	Missing	Impute start date as earliest possible date (i.e. first day of month if day unknown or 1st January if day and month are unknown), then: If stop date is missing could never be assumed a prior medication If start date <= end of treatment, assign as concomitant

START DATE	**STOP DATE**	**ACTION**
Missing	Known	If stop date < study med start date, assign as prior If stop date >= study med start date, assign as concomitant
	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 med start date, assign as prior If stop date >= study med start date, assign as concomitant
	Missing	Assign as concomitant

APPENDIX 4. **GEBOES SCORE COMPONENTS**

Grade 0: Architectural changes	0.0 No abnormality 0.1 Mild abnormality 0.2 Mild/moderate diffuse or multifocal abnormalities 0.3 Severe diffuse or multifocal abnormalities
Grade 1: Chronic inflammatory infiltrate	1.0 No increase 1.1 Mild but unequivocal increase 1.2 Moderate increase 1.3 Marked increase
Grade 2A: Eosinophils in lamina propria	2A.0 No increase 2A.1 Mild but unequivocal increase 2A.2 Moderate increase 2A.3 Marked increase
Grade 2B: Neutrophils in lamina propria	2B.0 No increase 2B.1 Mild but unequivocal increase 2B.2 Moderate increase 2B.3 Marked increase
Grade 3: Neutrophils in epithelium	3.0 None 3.1 < 5% crypts involved 3.2 < 50% crypts involved 3.3 > 50% crypts involved
Grade 4: Crypt destruction	4.0 None 4.1 Probable: local excess of neutrophils in part of the crypts 4.2 Probable: marked attenuation 4.3 Unequivocal crypt destruction
Grade 5: Erosions and ulcerations	5.0 No erosion, ulceration or granulation tissue 5.1 Recovering epithelium + adjacent inflammation 5.2 Probable erosion: focally stripped 5.3 Unequivocal erosion 5.4 Ulcer or granulation tissue

APPENDIX 5. **CONCOMITANT UC MEDICATIONS**

CATEGORY	**ATC Code value of WHODRUG**
AMINOSALICYLIC ACID AND SIMILAR AGENTS (5ASA)	A07EC
CORTICOSTEROIDS	A07EA, H02, D07BA, H02AB
IMMUNOSUPPRESSANTS	L04AD, L04AX, L01BB

Electronic Signature Manifestation

This page is a manifestation of the electronic signature(s) used in compliance with the organization's electronic signature policies and procedures.

Signer Full Name	Meaning of Signature	Date and Time
[redacted]	Document Approval (I certify that I have the education, training and experience to perform this task)	10 May 2021 14:23:18 UTC
[redacted]	Document Approval (I certify that I have the education, training and experience to perform this task)	10 May 2021 14:41:50 UTC
[redacted]	Document Approval (I certify that I have the education, training and experience to perform this task)	10 May 2021 14:45:57 UTC