STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 2, Blinded, Randomized, Placebo-Controlled Study Evaluating the Efficacy and Safety of GS-4875 in Subjects with Moderately to Severely Active Ulcerative Colitis
Name of Test Drug:	GS-4875
Study Number:	GS-US-365-4237
Protocol Version (Date):	Amendment 2 (19 June 2020)
Analysis Type:	Final Analysis
Analysis Plan Version:	1.0
Analysis Plan Date:	05 April 2021
Analysis Plan Author(s):	PPD

CONFIDENTIAL AND PROPRIETARY INFORMATION

TABLE OF CONTENTS

LIST OF IN-TEXT TABLES

LIST OF IN-TEXT FIGURES

LIST OF ABBREVIATIONS

AE	adverse event
BMI	body mass index
COVID-19	coronavirus disease 2019
CRF	case report form
CSR	clinical study report
CTCAE	Common Toxicity Criteria for Adverse Events
DMC	data monitoring committee
ECG	electrocardiogram
ET	early termination
FAS	Full Analysis Set
GDRC	Gilead Data Review Committee
HLGT	high-level group term
HLT	high-level term
hs-CRP	high-sensitivity C-reactive protein
ID	identification
LTT	lower-level term
LOQ	limit of quantitation
MCS	Mayo Clinic Score
MedDRA	Medical Dictionary for Regulatory Activities
NRI	non-responder imputation
OL	open-label
PE	physical examination
PGA	Physician's Global Assessment
PK	pharmacokinetic(s)
pMCS	partial Mayo Clinic Score
PT	preferred term
PTx	posttreatment
Q1, Q3	first quartile, third quartile
SAE	serious adverse events
SAP	statistical analysis plan
SD	standard deviation
SE	standard error
SOC	system organ class
TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
UC	ulcerative colitis
WHO	World Health Organization

1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical analysis methods and data presentations to be used in tables, figures, and listings (TFLs) in a synoptic clinical study report (CSR) for Study GS-US-365-4237. This SAP is based on the study protocol Amendment 2 dated 19 June 2020 and the electronic case report form (eCRF). The SAP will be finalized prior to data finalization for the primary analysis. Subject enrollment in Study GS-US-365-4237 was terminated early by Gilead. Data Monitoring Committee (DMC) meetings and Gilead Data Review Committee (GDRC) meetings will not be held for this study due to small number of subjects enrolled in this study. As well, some of the statistical analyses and all statistical testings planned in the study protocol will not be performed. Any changes made after the finalization of the SAP will be documented in the synoptic CSR.

1.1. Study Objectives

1.1.1. Primary Objectives

The primary objective of this study is as follows:

- To demonstrate the efficacy of GS-4875, compared with placebo control, in achieving Clinical Remission per Modified Mayo Clinic Score (MCS) at Week 10

1.1.2. Secondary Objectives

The secondary objectives of this study are as follows:

- To demonstrate the efficacy of GS-4875, compared with placebo control, in achieving endoscopic response at Week 10
- To demonstrate the efficacy of GS-4875, compared with placebo control, in achieving MCS Response at Week 10
- To demonstrate the efficacy of GS-4875, compared with placebo control, in achieving MCS Remission at Week 10
- To evaluate GS-4875, as compared with placebo control, in achieving histologic remission at Week 10
- To evaluate the safety and tolerability of GS-4875

CCI [redacted]

1.2. Study Design

This is a Phase 2, blinded, randomized, placebo-controlled study evaluating the efficacy and safety of GS-4875 for the treatment of subjects with moderately to severely active ulcerative colitis (UC). Adult male or female subjects 18 years of age or older who have documented evidence of UC and previously demonstrated an inadequate response or loss of response to a TNFα inhibitor may be eligible for entry (refer to the protocol for complete inclusion and exclusion criteria).

Approximately 180 subjects who meet protocol eligibility criteria will be randomized in a 1:1:1 ratio to 1 of 3 treatment groups as follows:

Treatment group 1 (n = 60): GS-4875 300 mg once daily

Treatment group 2 (n = 60): GS-4875 100 mg once daily

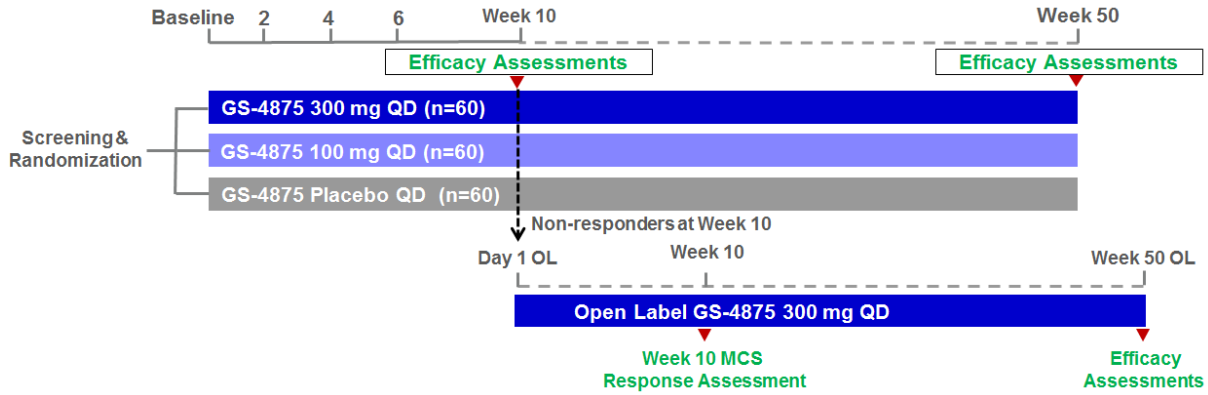
Treatment group 3 (n = 60): Placebo once daily

Central randomization is used. Treatment assignments will be stratified according to the sum (≤ 6 or > 6) of 3 MCS subscores for Stool Frequency, Rectal Bleeding, and Endoscopic Findings at Screening.

The study was terminated after 19 subjects were enrolled in the study.

A schematic of this study design is provided in Figure 1.

Figure 1. Study Schema



This study includes:

- Screening period (Days −30 to −1)
- Baseline/Randomization (Day 1)
- Blinded Treatment phase (Day 1 up to Week 50)
  - At Week 10 visit, all subjects will have an efficacy assessment.
  - Subjects who achieve MCS Response based on results from Week 10 will continue in the Blinded Treatment phase.
- Open-label Treatment phase (OL Day 1 up to OL Week 50)
  - All subjects who do not achieve MCS Response based on results from Week 10 will discontinue the Blinded Treatment phase and have the option to enter the OL Treatment phase.
  - At OL Week 10 visit, all subjects will have an efficacy assessment.
  - Subjects who achieve MCS Response based on results from OL Week 10 will continue in the OL Treatment phase. All subjects who do not achieve MCS Response will discontinue study drug.
- Posttreatment (PTx) Assessments

In the Blinded Treatment phase, randomized subjects may receive a maximum of 50 weeks of treatment. Subjects, who move to the OL Treatment phase, will have received 10 weeks of blinded treatment and may receive up to 50 weeks of OL treatment. Thus, total duration of treatment may be a maximum of 60 weeks.

Efficacy will be assessed primarily through modified MCS. MCS will be assessed at Screening, Blinded Treatment phase Week 10 and Week 50, and OL Treatment phase Week 10 and Week 50, if applicable.

Additional details on efficacy assessments are presented in Section 6, Appendix 1, and Appendix 2.

Safety will be assessed primarily through adverse events (AEs), laboratory analyses, electrocardiogram (ECG), physical examination (PE) and vital signs. Laboratory testing, PE and vital signs will be assessed at every visit.

Additional details on safety assessments are presented in Section 7, Appendix 1 and Appendix 2.

1.3. Sample Size and Power

A total of 180 subjects, i.e. 60 subjects in the placebo group and 60 subjects in each GS-4875 dose group (n = 120 total for GS-4875), will provide approximately 75% power when comparing each GS-4875 dose group to placebo at a 1-sided 0.025 significance level to detect a treatment difference in clinical remission rate per modified MCS of 17.5% (22.5% on GS-4875 and 5% on placebo) based on Fisher's exact test.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analyses

2.1.1. Planned Internal Unblinded Analysis

A Gilead internal unblinded team, the GS-US-365-4237 Gilead Data Review Committee (GDRC), independent of the blinded study team, was to perform the data review of study data after 90 subjects either complete the Week 10 visit or early discontinue from the study. Based on the interim analysis, the GDRC may propose changes in the study design, including potential termination of study due to lack of efficacy.

Ad hoc interim analyses at additional timepoints may also be requested, and data reviews be conducted by the GDRC, if needed.

The membership, conduct, and meeting schedule of the GDRC was to be specified in the GDRC Charter.

Due to small number of subjects enrolled in the study, the planned internal unblinded analysis to be reviewed by GDRC will not be performed.

2.1.2. DMC Analysis

An external multidisciplinary Data Monitoring Committee (DMC) was to review the progress of the study and perform interim reviews of the safety data in order to protect subject welfare and preserve study integrity. To ensure the best interests of the participants, the DMC was to make recommendations to the sponsor if the nature, frequency, and severity of adverse effects associated with the study treatment warrant the early termination of the study, the continuation of the study, or the continuation of the study with modifications.

The initial safety review was to be conducted after approximately 20 subjects either complete the Week 4 visit or discontinue from the study prior to Week 4. Subsequent DMC meetings for safety review was to be held after approximately 60 subjects either complete the Week 4 visit or discontinue from the study and after approximately 90 subjects either complete Week 10 visit or discontinue from the study. The frequency of meetings may be adjusted as requested by the DMC.

The DMC's role and responsibilities and the scope of analysis to be provided to the DMC were to be provided in a mutually agreed upon charter, which defines the DMC membership, meeting logistics, and meeting frequency.

Due to the fact that less than 20 subjects were enrolled in the study, no DMC meeting will be held for this study. The planned analysis to be reviewed by DMC will not be performed.

2.2. Primary Analysis

The unblinded primary analysis of the primary endpoint, i.e. Clinical Remission per Modified MCS, and secondary endpoints including safety was to be conducted when all randomized subjects (approximately 180) have completed Week 10 or discontinued from the study, and was to be tested at the 0.025 significance level.

Due to limited subject enrollment in the study, the unblinded primary analysis will be conducted for all randomized subjects. Some of the statistical analyses and all statistical testings planned in the study protocol will not be performed.

The analysis will be conducted after all subjects have completed 10 weeks of blinded study drug or discontinued from the study, associated safety and efficacy assessments have been completed, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized for the analysis.

2.3. Final Analysis

The unblinded final analysis will be performed after all subjects have completed the study, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized. The analysis of the other secondary endpoints CCI [redacted] will be conducted at the time of the final analysis.

Due to limited subject enrollment in the study, some of the statistical analyses and all statistical testings planned in the study protocol will not be performed.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

Analysis results will be presented using descriptive statistics. For categorical variables, the number and percentage of subjects in each category will be presented; for continuous variables, the number of subjects (n), mean, standard deviation (SD) or standard error (SE), median, first quartile (Q1), third quartile (Q3), minimum, and maximum will be presented.

By-subject listings will be presented for all subjects in the All Randomized Analysis Set and sorted by subject identification (ID) number, visit date, and time (if applicable). Data collected on log forms, such as AEs, will be presented in chronological order within the subject. The treatment group to which subjects were randomized or initially assigned will be used in the listings. Age, sex at birth, race, and ethnicity may be included in the listings, as space permits.

3.1. Analysis Sets

Analysis sets define the subjects to be included in an analysis. Analysis sets and their definitions are provided in this section. Subjects included in each analysis set will be determined before the study blind is broken for analysis. The analysis set will be identified and included as a subtitle of each table, figure, and listing.

For each analysis set, the number and percentage of subjects eligible for inclusion, as well as the number and percentage of subjects who were excluded and the reasons for their exclusion, will be summarized by treatment group.

3.1.1. All Randomized Analysis Set

The All Randomized Analysis Set includes all subjects who were randomized in the study.

This is the primary analysis set for by-subject listings.

3.1.2. Full Analysis Set

The Full Analysis Set (FAS) includes all randomized subjects who took at least 1 dose of study drug. This is the primary analysis set for efficacy analyses.

3.1.3. Safety Analysis Set

The Safety Analysis Set includes all subjects who took at least 1 dose of study drug. This is the primary analysis set for safety analyses.

CCI [redacted]

CCI [redacted]

3.1.6. Biomarker Analysis Set

The Biomarker Analysis Set includes all subjects in the FAS who have nonmissing baseline and at least 1 postbaseline measurement for at least 1 of the 3 biomarkers (high-sensitivity C-reactive protein [hs-CRP], fecal calprotectin, and fecal lactoferrin).

3.2. Subject Grouping

For analyses based on the All Randomized Analysis Sets and FAS, subjects will be grouped according to the treatment to which they were randomized. For analyses based on the Safety Analysis Set, and Biomarker Analysis Set, subjects will be grouped according to the actual treatment received. The actual treatment received will differ from the randomized treatment only when their actual treatment differs from randomized treatment for the entire treatment duration.

For subjects who entered the OL Treatment phase and took at least 1 dose of study drug (OL GS-4875), all data collected during the OL Treatment phase will be grouped according to the actual treatment received across the Blinded Treatment phase and OL Treatment phase, if applicable.

3.3. Strata and Covariates

Subjects will be randomly assigned to treatment groups via the interactive voice or web response system (IXRS) in a 1:1:1 ratio using a stratified randomization schedule. Stratification will be based on the sum (≤ 6 or > 6) of 3 MCS subscores for Stool Frequency, Rectal Bleeding, and Endoscopic Findings at Screening.

No stratification factors or covariates will be used in the analyses supporting the synoptic CSR.

3.4. Examination of Subject Subgroups

There are no prespecified subject subgroupings for efficacy and safety analyses.

3.5. Multiple Comparisons

No statistical testings will be performed. Adjustments for multiplicity will not be applied.

3.6. Missing Data and Outliers

3.6.1. Missing Data

In general, missing data will not be imputed unless methods for handling missing data are specified. Exceptions are presented in this document.

For missing last dosing date of study drug, imputation rules are described in Section 4.2.1. The handling of missing or incomplete dates for AE onset is described in Section 7.1.5.2.

3.6.2. Outliers

Outliers will be identified during the data management and data analysis process. All data, including outliers, will be included in analyses, unless otherwise specified.

3.7. Data Handling Conventions and Transformations

The following conventions will be used for the imputation of date of birth when it is partially missing or not collected:

- If only month and year of birth is collected, then "15" will be imputed as the day of birth
- If only year of birth is collected, then "01 July" will be imputed as the day and month of birth
- If year of birth is missing, then date of birth will not be imputed.

In general, age collected at Day 1 (in years) will be used for analyses and presented in listings. If age at Day 1 is not available for a subject, then age derived based on date of birth and the Day 1 visit date will be used instead. If an enrolled subject was not dosed with any study drug, the randomization date will be used instead of the Day 1 visit date. For screen failures, the date the first informed consent was signed will be used for the age derivation. Age required for longitudinal and temporal calculations and analyses (e.g., estimates of creatinine clearance, age at date of AE) will be based on age derived from date of birth and the date of the measurement or event, unless otherwise specified.

Non-PK data that are continuous in nature but are less than the lower limit of quantitation (LOQ) or above the upper LOQ will be imputed as follows:

- A value that is 1 unit less than the LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "< x" (where x is considered the LOQ). For example, if the values are reported as < 50 and < 5.0, values of 49 and 4.9, respectively, will be used to calculate summary statistics. An exception to this rule is any value reported as < 1 or < 0.1, etc. For values reported as < 1 or < 0.1, a value of 0.9 or 0.09, respectively, will be used to calculate summary statistics.

- A value that is 1 unit above the LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "> x" (where x is considered the LOQ). Values with decimal points will follow the same logic as above.

- The LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "≤ x" or "≥ x" (where x is considered the LOQ).

3.8. Analysis Visit Windows

3.8.1. Definition of Study Day

For all subjects who received at least 1 dose of study drug, Study Day will be calculated from the first dosing date of study drug and derived as follows:

- For postdose study days: Assessment Date – First Dosing Date + 1

- For days prior to the first dose: Assessment Date – First Dosing Date

Therefore, Study Day 1 is the day of first dose of study drug administration.

Baseline is defined as the last available observation on or prior to Study Day 1, unless otherwise specified.

For subjects who entered OL Treatment phase and received at least 1 dose of study drug (OL GS-4875), OL Study Day will be calculated from the first dosing date of study drug in OL Treatment phase and derived as follows:

- For postdose OL study days: Assessment Date – First Dosing Date of study drug in OL Treatment phase + 1

Therefore, OL (Study) Day 1 is the day of first dose of study drug administration in OL Treatment phase.

OL baseline is defined as the last available observation on or prior to OL Study Day 1, unless otherwise specified.

3.8.2. Analysis Visit Windows

Subject visits might not occur on protocol-specified days. Therefore, for the purpose of analysis, observations will be assigned to analysis windows.

Endoscopic Subscore

The analysis windows for Endoscopic Subscore are provided in Table 3-1 for Blinded Treatment phase and Table 3-2 for OL Treatment phase.

Table 3-1. Analysis Visit Windows for Endoscopic Subscore – Blinded Treatment Phase

Nominal Visit	Analysis Visit	Nominal Study Day	Visit Window Study Day	
			Lower Limit	Upper Limit
Screening	Baseline	(none)	(none)	1
Week 10	Week 10	71	58	minimum of 85 and OL Day 1 (if applicable)
Week 50	Week 50	351	324	379

Note: Anchor day defined in Appendix 4 will be used for analysis visit window calculation of MCS and all efficacy endpoints based on MCS; endoscopic day will be used for analysis visit window calculation of endoscopic subscore

Table 3-2. Analysis Visit Windows for Endoscopic Subscore – OL Treatment Phase

Nominal Visit	Analysis Visit	Nominal Study Day (OL Day)	Visit Window Study Day (OL Day)	
			Lower Limit	Upper Limit
OL Week 10	OL Week 10	71	58	85
OL Week 50	OL Week 50	351	324	379

Note: Anchor day defined in Appendix 4 will be used for analysis visit window calculation of MCS and all efficacy endpoints based on MCS; endoscopic day will be used for analysis visit window calculation of endoscopic subscore

Stool Frequency, Rectal Bleeding and Physician's Global Assessment (PGA) Subscores

The analysis windows for Stool Frequency, Rectal Bleeding and PGA subscores are provided in Table 3-3 for Blinded Treatment phase and Table 3-4 for OL Treatment phase.

Table 3-3. Analysis Visit Windows for Stool Frequency, Rectal Bleeding and PGA Subscores – Blinded Treatment Phase

Nominal Visit	Analysis Visit	Nominal Study Day	Visit Window Study Day	
			Lower Limit	Upper Limit
Screening/Day 1	Baseline	1	(none)	1
Week 2	Week 2	15	2	22
Week 4	Week 4	29	23	36
Week 6	Week 6	43	37	57
Week 10	Week 10	71	58	minimum of 85 and OL Day 1 (if applicable)
Week 14	Week 14	99	86	113
Week 18	Week 18	127	114	141
Week 22	Week 22	155	142	169
Week 26	Week 26	183	170	197
Week 30	Week 30	211	198	225
Week 34	Week 34	239	226	253
Week 38	Week 38	267	254	281
Week 42	Week 42	295	282	309
Week 46	Week 46	323	310	337
Week 50	Week 50	351	338	365

Note: Anchor day defined in Appendix 4 will be used for analysis visit window calculation of MCS and all efficacy endpoints based on MCS; endoscopic day will be used for analysis visit window calculation of endoscopic subscore

Table 3-4. Analysis Visit Windows for Stool Frequency, Rectal Bleeding and PGA Subscores – OL Treatment Phase

Nominal Visit	Analysis Visit	Nominal Study Day (OL Day)	Visit Window Study Day (OL Day)	
			Lower Limit	Upper Limit
OL Day 1	OL Day 1	1	1	1
OL Week 2	OL Week 2	15	2	22
OL Week 4	OL Week 4	29	23	36
OL Week 6	OL Week 6	43	37	57
OL Week 10	OL Week 10	71	58	85
OL Week 14	OL Week 14	99	86	113
OL Week 18	OL Week 18	127	114	141
OL Week 22	OL Week 22	155	142	169
OL Week 26	OL Week 26	183	170	197
OL Week 30	OL Week 30	211	198	225
OL Week 34	OL Week 34	239	226	253
OL Week 38	OL Week 38	267	254	281
OL Week 42	OL Week 42	295	282	309
OL Week 46	OL Week 46	323	310	337
OL Week 50	OL Week 50	351	338	365

Note: Anchor day defined in Appendix 4 will be used for analysis visit window calculation of MCS and all efficacy endpoints based on MCS; endoscopic day will be used for analysis visit window calculation of endoscopic subscore

Clinical Laboratory Assessments

The analysis windows for hematology, chemistry and urinalysis laboratory assessments are provided in Table 3-5 for Blinded Treatment phase and Table 3-6 for OL Treatment phase.

Table 3-5. Analysis Visit Windows for Hematology, Chemistry and Urinalysis Laboratory Assessments – Blinded Treatment Phase

Nominal Visit	Analysis Visit	Nominal Study Day	Visit Window Study Day	
			Lower Limit	Upper Limit
Screening/Day 1	Baseline	1	(none)	1
Week 2	Week 2	15	2	22
Week 4	Week 4	29	23	36
Week 6	Week 6	43	37	57
Week 10	Week 10	71	58	minimum of 85 and OL Day 1 (if applicable)
Week 14	Week 14	99	86	113
Week 18	Week 18	127	114	141
Week 22	Week 22	155	142	169
Week 26	Week 26	183	170	197
Week 30	Week 30	211	198	225
Week 34	Week 34	239	226	253
Week 38	Week 38	267	254	281
Week 42	Week 42	295	282	309
Week 46	Week 46	323	310	337
Week 50	Week 50	351	338	>351

Table 3-6. Analysis Visit Windows for Hematology, Chemistry and Urinalysis Laboratory Assessments – OL Treatment Phase

Nominal Visit	Analysis Visit	Nominal Study Day (OL Day)	Visit Window Study Day (OL Day)	
			Lower Limit	Upper Limit
OL Day 1	OL Baseline	1	(none)	1
OL Week 2	OL Week 2	15	2	22
OL Week 4	OL Week 4	29	23	36
OL Week 6	OL Week 6	43	37	57
OL Week 10	OL Week 10	71	58	85
OL Week 14	OL Week 14	99	86	113
OL Week 18	OL Week 18	127	114	141
OL Week 22	OL Week 22	155	142	169
OL Week 26	OL Week 26	183	170	197
OL Week 30	OL Week 30	211	198	225
OL Week 34	OL Week 34	239	226	253
OL Week 38	OL Week 38	267	254	281
OL Week 42	OL Week 42	295	282	309
OL Week 46	OL Week 46	323	310	337
OL Week 50	OL Week 50	351	338	>351

3.8.3. Selection of Data in the Event of Multiple Records in an Analysis Visit Window

Depending on the statistical analysis method, single values may be required for each analysis window. For example, change from baseline by visit usually requires a single value, whereas a time-to-event analysis would not require 1 value per analysis window.

If multiple valid, nonmissing measurements exist in an analysis window, records will be chosen based on the following rules if a single value is needed:

- For baseline, the last nonmissing value on or prior to the first dosing date of study drug will be selected, unless specified differently. If there are multiple records with the same time or no time recorded on the same day, the baseline value will be the average of the measurements for continuous data, or the measurement with the lowest severity (e.g., normal will be selected over abnormal for safety ECG findings) for categorical data.

- For postbaseline values:

  — The record closest to the nominal day for that visit will be selected.

  — If there are 2 records that are equidistant from the nominal day, the later record will be selected.

  — If there is more than 1 record on the selected day, the average will be taken for continuous data and the worse severity will be taken for categorical data, unless otherwise specified.

4. SUBJECT DISPOSITION

4.1. Subject Enrollment and Disposition

Key study dates (i.e., first subject screened, first subject randomized, last subject randomized, last subject last visit for the primary endpoint, and last subject last visit for the clinical study report) will be provided.

A summary of subject disposition will be provided by treatment group. This summary will present the number of subjects screened, the number of subjects randomized in Blinded Treatment phase, the number of subjects entered OL Treatment phase, and the number of subjects in each of the categories listed below:

- Safety Analysis Set
- Full Analysis Set
- Completed study drug dosing through Week 10 (indicated in Study Drug Completion CRF)
- Did not complete study drug up to Week 10 with reasons for premature discontinuation of study drug
- Continuing study drug (for analyses other than the final analysis)
- Completed study drug dosing through Week 50 (indicated in Study Drug Completion CRF)
- Continued Blinded Treatment phase after Week 10 but did not complete study drug up to Week 50 with reasons for premature discontinuation of study drug
- Entered OL Treatment phase after Week 10 and completed study drug dosing through OL Week 50 (indicated in Study Drug Completion CRF)
- Entered OL Treatment phase after Week 10 but did not complete study drug up to OL Week 50 with reasons for premature discontinuation of study drug
- Completed study
- Did not complete the study with reasons for premature discontinuation of study

For the status of study drug and study completion and reasons for premature discontinuation, the number and percentage of subjects in each category will be provided. The denominator for the percentage calculation will be the total number of subjects in the Safety Analysis Set corresponding to that column.

4.2. Extent of Study Drug Exposure and Adherence

Extent of exposure to study drug will be examined by assessing the total duration of exposure to study drug.

Summaries of extent of study drug exposure and adherence will be provided by:

- Blinded Treatment phase
- OL Treatment phase

4.2.1. Duration of Exposure to Study Drug

Total duration of exposure to study drug will be defined as last dosing date minus first dosing date plus 1, regardless of any temporary interruptions in study drug administration, and will be expressed in weeks using up to 1 decimal place (e.g., 4.5 weeks). If the last study drug dosing date is missing, the latest date among the study drug end date, clinical visit date, laboratory sample collection date, and vital signs assessment date that occurred during the on-treatment period will be used for subjects included in the final analyses or the last available date in the database snapshot for subjects who were still on treatment at the time of an interim analysis.

The total duration of exposure to study drug will be summarized using descriptive statistics and using the number (i.e., cumulative counts) and percentage of subjects exposed through the following time periods:

- Blinded Treatment phase: 1 day, 4 weeks, 6 weeks, 10 weeks, 14 weeks, 18 weeks, 22 weeks, 26 weeks, 30 weeks, 34 weeks, 38 weeks, 42 weeks, 46 weeks and 50 weeks
- OL Treatment phase: 1 day, 4 weeks, 6 weeks, 10 weeks, 14 weeks, 18 weeks, 22 weeks, 26 weeks, 30 weeks, 34 weeks, 38 weeks, 42 weeks, 46 weeks and 50 weeks

Summaries will be provided by treatment group for the Safety Analysis Set. No formal statistical testing is planned.

A by-subject listing of study drug administration will be provided separately by subject ID number (in ascending order) and visit (in chronological order).

4.3. Protocol Deviations

Subjects who did not meet the eligibility criteria for study entry but enrolled in the study, will be summarized regardless of whether they were exempted by the sponsor or not. A by-subject listing will be provided for those subjects who did not meet at least 1 eligibility (inclusion or exclusion) criterion. The listing will present the eligibility criterion (or criteria if more than 1 deviation) that subjects did not meet and related comments, if collected.

Protocol deviations occurring after subjects entered the study are documented during routine monitoring. A by-subject listing will be provided for those subjects with important protocol deviation.

This study was ongoing during the coronavirus disease 2019 (COVID-19) pandemic. A by-subject listing will be provided for subjects with important protocol deviations related to COVID-19, if applicable. A separate listing will be provided for subjects with non-important protocol deviation related to COVID-19.

5. BASELINE CHARACTERISTICS

5.1. Demographics and Baseline Characteristics

Subject demographic variables (i.e., age, sex, race, and ethnicity) and baseline characteristics (body weight [in kg], height [in cm], and body mass index [BMI; in kg/m^2]) will be summarized by treatment group and overall using descriptive statistics for continuous variables and using number and percentage of subjects for categorical variables. The summary of demographic data will be provided for the Safety Analysis Set.

A by-subject demographic listing, including the informed consent date, will be provided by subject ID number in ascending order.

5.2. Other Baseline Characteristics

The following baseline disease characteristics will be summarized by treatment group and overall using descriptive statistics for continuous variables and using number and percentage of subjects for categorical variables:

- Duration of UC (in years) from date of diagnosis to first dosing date
- MCS
- Partial MCS (pMCS)
- Endoscopic subscore of 3 (yes, no)

The summary of these baseline characteristics will be provided for the Safety Analysis Set. No formal statistical testing is planned.

A by-subject listing of baseline disease characteristics will be provided by subject ID number in ascending order. The following baseline disease characteristics will also be included in the listing:

- Extent of UC from medical history
- UC treatment history
  - Prior use of biologic agents (yes, no)
  - Number of TNFα antagonist used (1, 2, ≥ 3)
  - Prior use of vedolizumab (yes, no)
  - Prior use of ustekinumab (yes, no)

- UC concomitant medication

  — Systemically absorbed corticosteroids (yes, no)

5.3. Medical History

The extent of UC will be included in the by-subject listing of baseline disease characteristics. Other medical history data will not be summarized or listed.

6. EFFICACY ANALYSES

6.1. General Considerations

The efficacy analysis will be conducted on the FAS, defined in Section 3.1.2, unless otherwise specified.

The definitions for the key efficacy endpoints (i.e. primary and key secondary efficacy endpoints) are listed in Table 6-1. All of the key efficacy endpoints are dichotomous.

Table 6-1. Definitions for Primary and Key Secondary Efficacy Endpoints

Type	Event Endpoint	Definition
Primary	Clinical Remission per Modified MCS at Week 10	Stool Frequency subscore ≤ 1 and not greater than baseline, Rectal Bleeding subscore of 0, and Endoscopic subscore ≤ 1 at Week 10
Secondary	Endoscopic Response at Week 10	Endoscopic subscore ≤ 1 at Week 10
Secondary	MCS Response at Week 10	A decrease from baseline of ≥ 3 points and at least 30% in MCS, in addition to a ≥ 1 point decrease from baseline in the Rectal Bleeding subscore or a Rectal Bleeding subscore ≤ 1 at Week 10
Secondary	MCS Remission at Week 10	MCS score of ≤ 2 and no individual subscore > 1 at Week 10
Secondary	Histologic Remission at Week 10	Geboes Scale with all of the following must be met at Week 10: Grade 0 of ≤ 0.3, Grade 1 of ≤ 1.1, Grade 2a of ≤ 2A.3, Grade 2b of 2B.0, Grade 3 of 3.0, Grade 4 of 4.0, and Grade 5 of 5.0 {Geboes 2000}

For each of the key efficacy endpoints defined above, responders are subjects who achieved the endpoint based on assessment. Subjects who do not have sufficient measurements to determine the endpoint will be considered non-responders (i.e., non-responder imputation [NRI]).

MCS Response at Week 10 will be used to determine whether a subject is eligible to continue Blinded Treatment phase or enter OL Treatment phase. Subjects with insufficient data to assess MCS Response will discontinue study drug and are not eligible for the OL Treatment phase, even if they are considered as non-responder by NRI.

6.1.1. Calculations of MCS and pMCS with the Subscores

The MCS is an instrument designed to measure disease activity in UC (Table 6-2). The MCS system is a composite index of 4 disease activity variables. Each variable is scored individually on an integer scale of 0 to 3, inclusive, with higher scores indicating greater disease activity. The

individual components of the MCS include Stool Frequency, Rectal Bleeding, Endoscopic Findings subscore, and the Physician's Global Assessment (PGA). Stool Frequency and Rectal Bleeding are determined using an electronic daily diary, which collects subject reported components directly.

The efficacy endpoints described in Table 6-1, except for Histologic Remission, are all based on the 4 individual components. MCS is calculated as the sum of the 4 subscores, ranging from 0 to 12. A pMCS is calculated as the sum of the 3 subscores excluding the Endoscopic subscore, ranging from 0 to 9. Further information on the MCS and calculation rules are listed in Appendix 4.

Table 6-2. Modified Mayo Clinic Score (MCS)

Variables	Score			
	0	**1**	**2**	**3**
Stool Frequency	Normal number of stools for subject	1 to 2 stools per day more than normal	3 to 4 stools per day more than normal	≥ 5 stools per day more than normal
Rectal Bleeding	No blood seen	Streaks of blood with stool less than half the time	Obvious blood or streaks of blood with stool most of the time	Blood alone passes
Endoscopic Findings	Normal or inactive disease	Mild disease	Moderate disease	Severe disease
Physician Global Assessment	Normal	Mild disease	Moderate disease	Severe disease

A by-subject listing will be provided by subject ID number and visit for the following scores:

- MCS
- MCS subscores in Stool Frequency, Rectal Bleeding, Endoscopic Findings (locally and centrally read), and PGA
- pMCS

6.2. Primary Efficacy Endpoints

6.2.1. Definition of the Primary Efficacy Endpoints

The primary efficacy endpoint is the proportion of subjects achieving Clinical Remission per Modified MCS at Week 10, as defined in Table 6-1. MCS subscores collected at Screening will be used as baseline values.

6.2.2. Analysis of the Primary Efficacy Endpoint

Due to limited subject enrollment in the study, the summary of primary efficacy endpoint will not be provided. No statistical testing will be performed. A by-subject listing of Clinical Remission status per Modified MCS at Week 10 will be provided by subject ID number.

6.3. Secondary Efficacy Endpoints

6.3.1. Definition of the Secondary Efficacy Endpoints

The key secondary efficacy endpoints are:

- The proportion of subjects with Endoscopic Response at Week 10
- The proportion of subjects with MCS Response at Week 10
- The proportion of subjects with MCS Remission at Week 10
- The proportion of subjects with Histologic Remission at Week 10

6.3.2. Analysis of the Secondary Efficacy Endpoint

Due to limited subject enrollment in the study, the summary of secondary efficacy endpoints will not be provided. No statistical testing will be performed. A by-subject listing of response status will be provided for the following secondary efficacy endpoints:

- Endoscopic Response (yes, no) at Week 10
- MCS Response (yes, no) at Week 10
- MCS Remission (yes, no) at Week 10

Histologic data will not be read or processed. Consequently, Histologic Remission (yes, no) at Week 10 will not be listed.

CCI [redacted]

[redacted]

7. SAFETY ANALYSES

7.1. Adverse Events and Deaths

If an AE occurred in Blinded Treatment phase, this AE will be summarized under blinded treatment group. For subjects who entered OL Treatment phase, an AE will be summarized under OL treatment if this AE start date is on or after the first dose of OL treatment.

7.1.1. Adverse Event Dictionary

Clinical and laboratory AEs will be coded using the current version of Medical Dictionary for Regulatory Activities (MedDRA). System organ class (SOC), high-level group term (HLGT), high-level term (HLT), preferred term (PT), and lower-level term (LLT) will be provided in the AE dataset.

7.1.2. Adverse Event Severity

Adverse events are graded by the investigator as Grade 1, 2, 3, 4, or 5 according to toxicity criteria specified in the protocol. The severity grade of events for which the investigator did not record severity will be categorized as "missing" for tabular summaries and data listings. The missing category will be listed last in summary presentation.

7.1.3. Relationship of Adverse Events to Study Drug

Related AEs are those for which the investigator selected "Related" on the AE CRF to the question of "Related to Study Treatment." Relatedness will always default to the investigator's choice, not that of the medical monitor. Events for which the investigator did not record relationship to study drug will be considered related to study drug for summary purposes. However, by-subject data listings will show the relationship as missing.

7.1.4. Serious Adverse Events

Serious adverse events (SAEs) will be identified and captured as SAEs if the AEs met the definitions of SAEs that were specified in the study protocol. SAEs captured and stored in the clinical database will be reconciled with the SAE database from the Gilead Drug Safety and Public Health Department before data finalization.

7.1.5. Treatment-Emergent Adverse Events

7.1.5.1. Definition of Treatment-Emergent Adverse Events

Treatment-emergent adverse events (TEAEs) for the Blinded Treatment phase are defined as 1 or both of the following:

- Any AEs with an onset date on or after the Blinded Treatment phase study drug start date and no later than 30 days after permanent discontinuation of the Blinded Treatment phase study drug if no OL Treatment phase study drug was taken, OR any AEs with an onset date on or after the Blinded Treatment phase study drug start date and before the OL Treatment phase study drug start date if OL Treatment phase study drug was taken.

- Any AEs leading to premature discontinuation of Blinded Treatment phase study drug.

TEAEs for the OL Treatment phase are defined as 1 or both of the following:

- Any AEs with an onset date on or after the OL Treatment phase study drug start date and no later than 30 days after permanent discontinuation of the OL Treatment phase study drug.

- Any AEs leading to premature discontinuation of OL Treatment phase study drug.

7.1.5.2. Incomplete Dates

If the onset date of the AE is incomplete and the AE stop date is not prior to the first dosing date of study drug, then the month and year (or year alone if month is not recorded) of onset determine whether an AE is treatment emergent. The event is considered treatment emergent if both of the following 2 criteria are met:

- The AE onset is the same as or after the month and year (or year) of the first dosing date of study drug, and

- The AE onset date is the same as or before the month and year (or year) of the date corresponding to 30 days after the date of the last dose of study drug

An AE with completely missing onset and stop dates, or with the onset date missing and a stop date later than the first dosing date of study drug, will be considered to be treatment emergent. In addition, an AE with the onset date missing and incomplete stop date with the same or later month and year (or year alone if month is not recorded) as the first dosing date of study drug will be considered treatment emergent.

7.1.6. Summaries of Adverse Events and Deaths

Treatment-emergent AEs will be summarized based on the Safety Analysis Set.

7.1.6.1. Summaries of AE Incidence in Combined Severity Grade Subsets

A brief, high-level summary of the number and percentage of subjects who experienced at least 1 TEAE in the categories described below will be provided by treatment group. All deaths observed in the study will also be included in this summary.

- TEAE
- TEAEs with Grade 3 or higher
- TEAEs with Grade 2 or higher
- TE treatment-related AEs
- TE treatment-related AEs with Grade 3 or higher
- TE SAEs
- TE treatment-related SAEs
- TEAEs leading to premature discontinuation of study drug

The number and percentage of subjects who experienced at least 1 TEAE will be provided and summarized by PT and treatment group. For the other AE categories described below, summaries will be provided by SOC, PT, and treatment group:

- TE treatment-related AEs
- TE SAEs
- TEAEs leading to premature discontinuation of study drug

Multiple events will be counted only once per subject in each summary. Adverse events will be summarized and listed first in alphabetic order of SOC within each SOC (if applicable), and then by PT in descending order of total frequency within each SOC. For summaries by severity grade, the most severe grade will be used for those AEs that occurred more than once in an individual subject during the study.

Data listings will be provided for the following:

- All AEs, indicating whether the event is treatment emergent
- All SAEs
- All Deaths
- All AEs leading to premature discontinuation of study drug

7.2. Laboratory Evaluations

Laboratory data collected during the study will be analyzed and summarized using both quantitative and qualitative methods. Summaries of laboratory data will be provided for the Safety Analysis Set and will include data collected up to the last dose of study drug plus 30 days for subjects who have permanently discontinued study drug. The analysis will be based on values reported in conventional units. When values are below the LOQ, they will be listed as such, and the closest imputed value will be used for the purpose of calculating summary statistics as specified in Section 3.7. Hemolized test results will not be included in the analysis, but they will be listed in by-subject laboratory listings.

A by-subject listing for laboratory test results will be provided by subject ID number and time point in chronological order for hematology, serum chemistry, and urinalysis separately. Values falling outside of the relevant reference range and/or having a severity grade of 1 or higher on the CTCAE severity grade will be flagged in the data listings, as appropriate.

No formal statistical testing is planned.

7.2.1. Summaries of Numeric Laboratory Results

Descriptive statistics for laboratory tests will not be provided.

7.2.2. Graded Laboratory Values

The CTCAE Version 5.0 will be used to assign toxicity grades (0 to 4) to laboratory results for analysis. Grade 0 includes all values that do not meet the criteria for an abnormality of at least Grade 1. For laboratory tests with criteria for both increased and decreased levels, analyses for each direction (i.e., increased, decreased) will be presented separately.

7.2.2.1. Treatment-Emergent Laboratory Abnormalities

Treatment-emergent laboratory abnormalities for Blinded Treatment phase are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point,

- up to and including the date of last dose of Blinded Treatment phase study drug plus 30 days for subjects who permanently discontinued Blinded Treatment phase study drug
- or before the first dose of OL Treatment phase study drug for subjects who entered OL Treatment phase

For subjects who entered the OL Treatment phase, treatment-emergent laboratory abnormalities for OL Treatment phase are defined as values that increase at least 1 toxicity grade from OL baseline at any postbaseline time point, up to and including the date of last dose of OL Treatment phase study drug plus 30 days for subjects who permanently discontinued OL phase study drug.

If the relevant baseline laboratory value is missing, any abnormality of at least Grade 1 observed within the time frame specified above will be considered treatment emergent.

7.2.2.2. Summaries of Laboratory Abnormalities

Laboratory data that are categorical will be summarized using the number and percentage of subjects in the study with the given response at baseline and each scheduled postbaseline time point for both Blinded Treatment phase and OL Treatment phase.

The following summary (number and percentage of subjects) for treatment-emergent laboratory abnormalities will be provided by laboratory test and treatment group; subjects will be categorized according to the most severe postbaseline abnormality grade for a given laboratory test:

- Graded laboratory abnormalities

For all summaries of laboratory abnormalities, the denominator is the number of subjects with nonmissing postbaseline values.

7.3. Body Weight and Vital Signs

Body weight and vital signs will not be summarized or listed.

7.4. Prior and Concomitant Medications

Medications collected at screening and during the study will be coded using the current version of the World Health Organization (WHO) Drug dictionary.

UC-specific prior and concomitant medications at baseline will be included in the listing of other baseline characteristics as described in Section 5.2. No other prior and concomitant medications will be summarized or listed.

7.4.1. Prior Medications

Prior medications are defined as any medications taken before a subject took the first study drug.

For the purposes of analysis, any UC-specific medication with a start date prior to the first dosing date of study drug will be included in the UC treatment history summary in the listing of other baseline characteristics as described in Section 5.2, regardless of when the stop date is. If a partial start date is entered the medication will be considered prior unless the month and year (if day is missing) or year (if day and month are missing) of the start date are after the first dosing date. Medications with a completely missing start date will be included in the UC treatment history summary, unless otherwise specified.

7.4.2. Concomitant Medications

Concomitant medications are defined as medications taken while a subject took study drug.

For the purposes of analysis, any UC-specific medications with a start date prior to or on the first dosing date of study drug and continued to be taken after the first dosing date, or started after the first dosing date but prior to or on the last dosing date of study drug will be considered concomitant medications. Medications started and stopped on the same day as the first dosing date or the last dosing date of study drug will also be considered concomitant. Medications with a stop date prior to the date of first dosing date of study drug or a start date after the last dosing date of study drug will be excluded from the UC concomitant medication summary in the listing of other baseline characteristics as described in Section 5.2. If a partial stop date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) prior to the date of first study drug administration will be excluded from the UC concomitant medication summary. If a partial start date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) after the study drug stop date will be excluded from the UC concomitant medication summary. Medications with completely missing start and stop dates will be included in the UC concomitant medication summary, unless otherwise specified.

7.5. Electrocardiogram Results

Electrocardiogram (ECG) data will not be summarized or listed.

7.6. Other Safety Measures

A data listing will be provided for subjects who become pregnant during the study.

7.7. Changes From Protocol-Specified Safety Analyses

Due to limited subject enrollment in the study, only part of safety summaries and listings planned in the protocol will be provided.

[redacted]

9. BIOMARKER ANALYSES

The biological marker analysis will be conducted on the Biomarker Analysis Set, defined in Section 3.1.6.

A by-subject listing will be provided for serum hs-CRP, fecal calprotectin, and fecal lactoferrin by subject ID number and visit.

10. REFERENCES

Geboes K, Riddell R, Ost A, Jensfelt B, Persson T, Lofberg R. A reproducible grading scale for histological assessment of inflammation in ulcerative colitis. Gut 2000;47 (3):404-9.

11. SOFTWARE

SAS® Software Version 9.4. SAS Institute Inc., Cary, NC, USA.

nQuery Advisor(R) Version 8.6. Statistical Solutions, Cork, Ireland.

12. SAP REVISION

Revision Date (DD MMM YYYY)	Section	Summary of Revision	Reason for Revision
(n/a)	(n/a)	(n/a)	(n/a)

13. APPENDICES

Appendix 1. Study Procedures Table – Blinded Treatment

Period	Screen		Blinded Treatment														Follow-up	
Week		**0**	**2**	**4**	**6**	**10**	**14**	**18**	**22**	**26**	**30**	**34**	**38**	**42**	**46**	**50**	**PTx**	**ET**
Study Day	**-30 to -1**	**1**	**15**	**29**	**43**	**71**	**99**	**127**	**155**	**183**	**211**	**239**	**267**	**295**	**323**	**351**		
Visit Window			**±3**	**±3**	**±3**	**±5**	**±5**	**±5**	**±5**	**±5**	**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±3**	
Informed Consent	X																	
12-lead ECG	X					X					X					X		X
Physical Exam	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Review of Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Review of Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Study Drug Dispensing		X		X	X	X	X	X	X	X	X	X	X	X	X			
Colonoscopy/Flexible Sigmoidoscopy with Biopsies	X					X										X		
PGA for MCS Calculation	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X
Evaluation of Disease Worsening using Partial MCS							X	X	X	X	X	X	X	X	X			
eDiary instruction & review	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Stool Sample for Enteric Infections	X																	
Stool Biomarker Samples	X					X				X						X		
Urinalysis	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine Biomarker Samples	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy Test	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
TB Assessment	X																	

Period	Screen		Blinded Treatment														Follow-up	
Week		**0**	**2**	**4**	**6**	**10**	**14**	**18**	**22**	**26**	**30**	**34**	**38**	**42**	**46**	**50**	**PTx**	**ET**
Study Day	**-30 to -1**	**1**	**15**	**29**	**43**	**71**	**99**	**127**	**155**	**183**	**211**	**239**	**267**	**295**	**323**	**351**		
Visit Window			**±3**	**±3**	**±3**	**±5**	**±5**	**±5**	**±5**	**±5**	**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±3**	
HBV, HCV, HIV screening	X																	
HBV Monitoring, As Needed						X			X			X			X			
Hematology & Chemistry	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Fasting Lipids		X	X			X				X						X		
Blood Biomarker Samples		X	X	X		X				X						X		
Mandatory Genomic Samples		X																
CCI																		
CCI																		
CCI																		
HRQoL Surveys		X				X										X		
HCRU Questionnaire		X	X	X	X	X		X		X		X		X		X		
Approximate Total Amount of Blood Taken at This Visit	23.5 mL	44.5 mL	34.0 mL	34.0 mL	12.0 mL	34.0 or 40.0 mL	8.0 mL	8.0 mL	8.0 or 14.0 mL	30.0 mL	8.0 mL	8.0 or 14.0 mL	8.0 mL	8.0 mL	8.0 or 14.0 mL	30.0 mL	8.0 mL	8.0 mL

Appendix 2. Study Procedures Table – Open-Label Treatment

Period	**Open-Label Treatment**															**Follow-up**	
Week	**0**	**2**	**4**	**6**	**10**	**14**	**18**	**22**	**26**	**30**	**34**	**38**	**42**	**46**	**50**	**PTx**	**ET**
Study Day	**1**	**15**	**29**	**43**	**71**	**99**	**127**	**155**	**183**	**211**	**239**	**267**	**295**	**323**	**351**		
Visit Window		**±3**	**±3**	**±3**	**±5**	**±5**	**±5**	**±5**	**±5**	**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±3**	
12-lead ECG					X					X					X		X
Physical Exam	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Review of Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Review of Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Study Drug Dispensing	X		X	X	X	X	X	X	X	X	X	X	X	X			
Colonoscopy/Flexible Sigmoidoscopy with Biopsies					X										X		
PGA for MCS Calculation	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X
Evaluation for Disease Worsening using Partial MCS						X	X	X	X	X	X	X	X	X			
eDiary instruction & review	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Stool Biomarker Samples					X				X						X		
Urinalysis	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine Biomarker Samples	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy Test	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
HBV Monitoring					X			X			X			X			
Hematology & Chemistry	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Fasting Lipids					X				X						X		
Blood Biomarker Samples	X	X	X		X				X						X		
HRQoL Surveys	X				X										X		

Period	**Open-Label Treatment**															**Follow-up**	
Week	**0**	**2**	**4**	**6**	**10**	**14**	**18**	**22**	**26**	**30**	**34**	**38**	**42**	**46**	**50**	**PTx**	**ET**
Study Day	**1**	**15**	**29**	**43**	**71**	**99**	**127**	**155**	**183**	**211**	**239**	**267**	**295**	**323**	**351**		
Visit Window		**±3**	**±3**	**±3**	**±5**	**±5**	**±5**	**±5**	**±5**	**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±3**	
HCRU Questionnaire	X	X	X	X	X		X		X		X		X		X		
Approximate Total Amount of Blood Taken at This Visit	30.0 mL	34.0 mL	34.0 mL	12.0 mL	34.0 or 40.0 mL	8.0 mL	8.0 mL	8.0 or 14.0 mL	30.0 mL	8.0 mL	8.0 or 14.0 mL	8.0 mL	8.0 mL	8.0 or 14.0 mL	30.0 mL	8.0 mL	8.0 mL

Appendix 3. Modified Mayo Scoring System for Assessment of Ulcerative Colitis Activity

Stool Frequency – *Each subject serves as his or her own control to establish the degree of abnormality of the stool frequency*	☐ 0	Normal number of stools for subject
	☐ 1	1 to 2 stools per day more than normal
	☐ 2	3 to 4 stools per day more than normal
	☐ 3	≥ 5 stools per day more than normal
Rectal Bleeding – *The daily bleeding score represents the most severe bleeding of the day.*	☐ 0	No blood seen
	☐ 1	Streaks of blood with stool less than half the time
	☐ 2	Obvious blood (more than just streaks) or streaks of blood with stool most of the time
	☐ 3	Blood alone passes
Endoscopic findings – *Assessed by Central Reader (include only for MCS assessment)*	☐ 0	Normal or inactive disease
	☐ 1	Mild Disease *(erythema, decreased vascular pattern)*
	☐ 2	Moderate Disease *(marked erythema, lack of vascular pattern, friability, erosions)*
	☐ 3	Severe Disease *(spontaneous bleeding, ulceration)*
Physician's Global Assessment – *The physician's global assessment acknowledges the three other criteria, the subject's daily recollection of abdominal discomfort and general sense of well-being, and other observation, such as physical findings and the subject's performance status.*	☐ 0	Normal
	☐ 1	Mild disease
	☐ 2	Moderate disease
	☐ 3	Severe disease

Appendix 4. Mayo Clinic Score Calculation

Definition of the Mayo Clinic Score and Component Subscores

The (Modified) Mayo Clinic Score (MCS) is a composite index of 4 disease activity variables in stool frequency, rectal bleeding, endoscopic findings, and the physician global assessment (PGA). Each of the 4 variables is assigned an integer subscore from 0 – 3 as described in Table 6-2 and Appendix 3.

The MCS is calculated as the sum of the 4 subscores for stool frequency, rectal bleeding, endoscopic findings, and the PGA.

Partial MCS (pMCS) is the sum of the 3 subscores for stool frequency, rectal bleeding, and the PGA.

Calculation of Mayo Clinic Score and Component Subscores

Subjects report daily stool frequency and rectal bleeding symptoms on the study electronic diary. Results of endoscopic evaluation are reported by a central reader and site personnel enters the score on the web diary. PGA is recorded by the investigator for specified visits.

For the purposes of calculation of the specific MCS and component subscores an anchor date is assigned and stool frequency and rectal bleeding records prior to the anchor date are used in the calculation of the subscores.

For MCS calculation at Screening, the anchor date is considered the date of the endoscopy as endoscopic subscore will be only evaluated over screening period and not at Day 1 baseline. Screening MCS will be used as baseline evaluation.

For all calculations at other visits, including baseline pMCS, postbaseline MCS and postbaseline pMCS, the anchor date is the study visit date.

Because the preparation for endoscopy procedure may impact the validity of the diary data, the patients reported daily stool frequency and rectal bleeding records collected 1 day prior to, the day of, and the day after the procedure will not be used in the calculation of stool frequency and rectal bleeding subscores. These above mentioned days are considered as non-evaluable days for those 2 subscores.

Calculation of MCS at Screening (Baseline)

The calculation of the screening stool frequency subscore and screening rectal bleeding subscore for the purposes of calculation of MCS at Screening is as follows:

1) The endoscopic procedure date is defined as the E-Day 1.

2) A 7-day window is defined in which the start of the window begins 7 days prior to the endoscopic procedure date and the window ends on the day prior to the endoscopic procedure date.

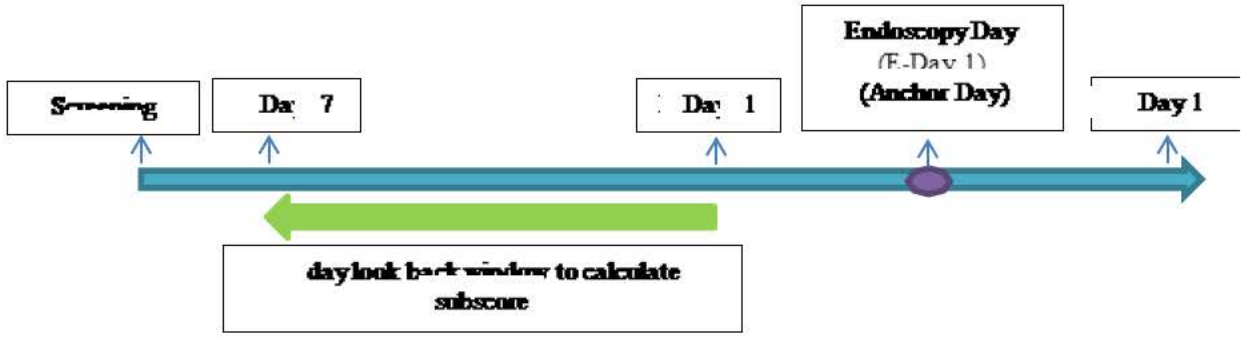
3) The subscore is calculated as the average of the 3 evaluable diary data entries within the 7-day window closest to the endoscopic procedure date (discarding the day prior to endoscopy) and rounded to the nearest integer.

4) If a subject does not have 3 or more evaluable diary day entries within the 7-day window, this subject will have a missing subscore and missing baseline MCS at Screening.

5) The PGA subscore used in the MCS at Screening is that recorded during the screening period (prior to Day 1) .

A schema of this approach (Appendix Figure 1) and examples (Appendix Table 1) are provided below:

Appendix Figure 1. Stool Frequency and Rectal Bleeding Subscores Calculation at Screening



Appendix Table 1. Examples of Stool Frequency and Rectal Bleeding Subscores Calculation for MCS at Screening

	Diary Day Looking Back from Endoscopy Date (E-Day)							Anchor Day			
	-7	-6	-5	-4	-3	-2	-1	E-Day 1			
Example	3 Jun	4 Jun	5 Jun	6 Jun	7 Jun	8 Jun	9 Jun	10 Jun	Days for Calculation	Average Subscore	Final Subscore
Diary 1	M	M	2	M	1	2	X	X	-2, -3, -5	1.67	2
Diary 2	M	M	M	M	0	1	X	X	-2, -3	Missing	Missing
Diary 3	M	M	M	M	0	M	X	X	-3	Missing	Missing
Diary 4	M	2	M	2	1	1	X	X	-2, -3, -4	1.33	1

Days are named relative to Anchor Day Endoscopy Date (E-Day 1), M = Missing, X = non-evaluable. The diary data collected on E-Day 1 and E-Day -1 will be discarded as endoscopy and its preparation may impact the validity of the diary data.

Calculation of Postbaseline MCS, Baseline and Postbaseline pMCS

The calculation of postbaseline MCS, baseline and postbaseline pMCS use the study visit date as the anchor date. The calculations are as follows:

1) Subject diary data collected within 7 days prior to the visit day will be used for calculation, and some of the days within this 7-day window may be considered non-evaluable due to the endoscopy procedure and its preparation (i.e., the day of the endoscopy and the day prior to or after the endoscopy).

2) The average of the 3 evaluable diary day entries within the 7-day window closest to the visit day (V-Day 1), rounded to the nearest integer, will be considered the stool frequency and rectal bleeding subscore for that visit.

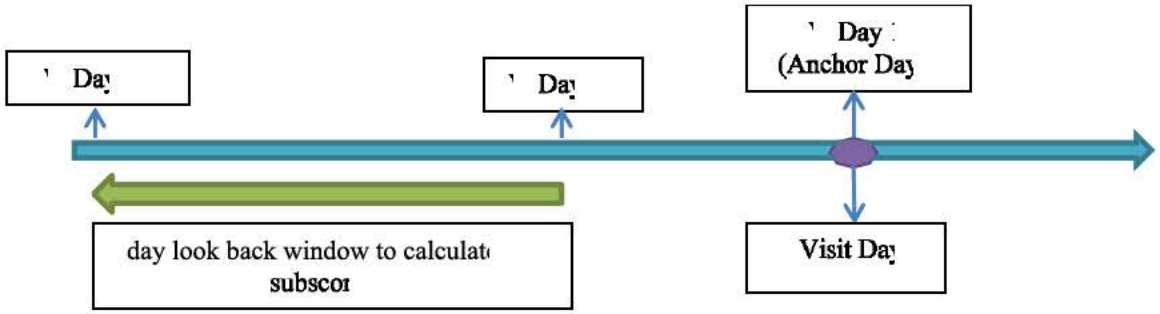
3) The PGA subscore used in the calculation of baseline pMCS is the PGA subscore recorded on Day 1. At subsequent postbaseline visits, the PGA subscore used in calculation of MCS and pMCS is that recorded within the visit window.

4) If there are 2 or less evaluable diary day entries for stool frequency or rectal bleeding within the 7-day window, no missing data imputation will be done. MCS and pMCS will be considered as missing.

5) For MCS, if endoscopic subscore or PGA subscore is missing, MCS will be left as missing. For pMCS, if PGA is missing, pMCS will be left as missing.

A schema of this approach (Appendix Figure 2) and examples (Appendix Table 2) are provided below:

Appendix Figure 2. Stool Frequency and Rectal Bleeding Subscores Calculation at Baseline and Postbaseline



Appendix Table 2. Examples of Stool Frequency and Rectal Bleeding Subscores Calculation for MCS at Postbaseline, and pMCS at Baseline and Postbaseline

	Diary Day Looking Back from Visit Date (V-Day)							Anchor Day			
	-7	-6	-5	-4	-3	-2	-1	V-Day 1			
Example	3 Jun	4 Jun	5 Jun	6 Jun	7 Jun	8 Jun	9 Jun	10 Jun	Days for Calculation	Average Subscore	Final Subscore
Diary 1	E	X	3	M	M	M	0	X	-1, -5	Missing	Missing
Diary 2	4	4	X	E	X	3	3	X	-1, -2, -6	3.33	3
Diary 3	3	X	E	X	1	M	2	X	-1, -3, -7	2	2
Diary 4	2	3	4	4	X	E	X	X	-4, -5, -6	3.67	4
Diary 5	2	M	M	X	E	X	2	X	-1, -7	Missing	Missing
Diary 6	X	E	X	2	3	0	1	X	-1, -2, -3	1.33	1
Diary 7	M	3	X	E	X	M	M	X	-6	N/A	Missing

Days are named relative to Anchor Day Visit Date (V-Day 1), M = Missing, X = non-evaluable, E = Endoscopy Day

GS-US-365-4237 Final SAP

ELECTRONIC SIGNATURES

Signed by	Meaning of Signature	Server Date (dd-MMM-yyyy hh:mm:ss)
PPD	Biostatistics eSigned	06-Apr-2021 15:01:37
PPD	Clinical Research eSigned	06-Apr-2021 20:30:50