STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of GS-9883/Emtricitabine/Tenofovir Alafenamide Versus Dolutegravir + Emtricitabine/Tenofovir Alafenamide in HIV-1 Infected, Antiretroviral Treatment-Naïve Adults
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CONFIDENTIAL AND PROPRIETARY INFORMATION

TABLE OF CONTENTS

TABLE OF CONTENTS 2
LIST OF ABBREVIATIONS 5
1. INTRODUCTION 7
1.1. Study Objectives 7
1.2. Study Design 7
1.3. Sample Size and Power 10
2. TYPE OF PLANNED ANALYSIS 11
2.1. Data Monitoring Committee Analyses 11
2.2. Interim Analyses 11
2.2.1. Week 48 Analysis 11
2.2.2. Week 96 Analysis 11
2.2.3. Week 144 Analysis 11
2.2.4. Open Label Week 48 Analysis 11
2.3. Final Analysis 11
3. GENERAL CONSIDERATIONS FOR DATA ANALYSES 12
3.1. Analysis Sets 13
3.1.1. All Randomized Analysis Set 13
3.1.2. All B/F/TAF Analysis Set 14
3.2. Subject Grouping 14
3.3. Strata and Covariates 14
3.4. Examination of Subject Subgroups 14
3.4.1. Subject Subgroups for Safety Analyses 14
3.5. Multiple Comparisons 15
3.6. Missing Data and Outliers 15
3.6.1. Missing Data 15
3.6.2. Outliers 15
3.7. Data Handling Conventions and Transformations 15
3.8. Analysis Windows 16
3.8.1. Definition of Study Day 16
3.8.2. Analysis Windows 17
3.8.3. Selection of Data in the Event of Multiple Records in an Analysis Window 23
4. SUBJECT DISPOSITION 25
4.1. Subject Enrollment and Disposition 25
4.1.1. Subject Enrollment 25
4.1.2. Subject Disposition 25
4.2. Extent of Study Drug Exposure and Adherence 26
4.2.1. Duration of Exposure to Study Drug 26
4.2.2. Adherence to Study Drug Regimen 26
4.3. Protocol Deviations 27
4.4. Missing Protocol-Specified Information due to COVID-19 28
5. BASELINE CHARACTERISTICS 29
5.1. Demographics and Baseline Characteristics 29
5.2. Baseline Disease Characteristics 29
5.3. Medical History 29
6. EFFICACY ANALYSES 30

6.1. Primary Efficacy Endpoint 30
6.2. Secondary Efficacy Endpoints 30
6.2.1. Definition of the Secondary Efficacy Endpoints 30
6.3. Efficacy Endpoints for all B/F/TAF Analysis 31
6.3.1. Definition of the Efficacy Endpoint for all B/F/TAF analysis 31
6.3.2. Analysis of the Efficacy Endpoints for All B/F/TAF Analysis 31
6.4. Changes from Protocol-Specified Efficacy Analyses 32

7. SAFETY ANALYSES 33

7.1. Adverse Events and Deaths 33
7.1.1. Adverse Event Dictionary 33
7.1.2. Adverse Event Severity 33
7.1.3. Relationship of Adverse Events to Study Drug 33
7.1.4. Serious Adverse Events 33
7.1.5. Treatment-Emergent Adverse Events 34
7.1.6. Summaries of Adverse Events and Death 34
7.1.7. Additional Analysis of Adverse Events 35
7.2. Laboratory Evaluations 36
7.2.1. Summaries of Numeric Laboratory Results 37
7.2.2. Graded Laboratory Values 37
7.2.3. Metabolic Laboratory Evaluations 39
7.2.4. Liver-Related Laboratory Evaluations 39
7.2.5. Renal-Related Laboratory Evaluations 40
7.3. Body Weight, Height, and Vital Signs 40
7.4. Prior and Concomitant Medications 40
7.4.1. Nonstudy Drug Antiretroviral Medications 40
7.4.2. Concomitant Non-ARV Medications 41
7.5. Electrocardiogram Results 41
7.6. Other Safety Measures 42
7.7. Changes from Protocol-Specified Safety Analyses 42

8. PHARMACOKINETIC ANALYSES 43

9. SPECIAL POPULATION ANALYSES 44

9.1. Analyses for HIV/HBV Coinfected Subjects 44
9.2. Analyses for HIV/HCV Coinfected Subjects 45

10. REFERENCES 46

11. SOFTWARE 47

12. SAP REVISION 48

13. APPENDICES 49

Appendix 1. Study Procedures Table 50
Appendix 2. Cardiovascular or Cerebrovascular Events 55
Appendix 3. Hepatic Events 56
Appendix 4. Adverse Events of COVID-19 57
Appendix 5. Determining Missing and Virtual Visits Due to COVID-19 58
Appendix 6. Programming Specification 61

LIST OF IN-TEXT TABLES

Table 3-1. Analysis Windows for HIV-1 RNA, CD4+ cell count, CD4 %, HBV DNA, Hematology, Chemistry, Urinalysis, Urine Pregnancy Laboratory Tests, $eGFR_{CG}$, Vital Signs, and Weight for the Randomized Phase Analysis....18
Table 3-2. Analysis Windows for HIV-1 RNA, CD4+ cell count, CD4 %, HBV DNA, Hematology, Chemistry, Urinalysis, and Urine Pregnancy Laboratory Tests, $eGFR_{CG}$, Vital Signs, and Weight for the All B/F/TAF Analysis....19
Table 3-3. Analysis Windows for Metabolic Assessments and HBV Serology for the Randomized Phase Analysis....20
Table 3-4. Analysis Windows for Metabolic Assessments and HBV Serology for the All B/F/TAF Analysis....20
Table 3-5. Analysis Windows for TSH for the Randomized Phase Analysis....21
Table 3-6. Analysis Windows for TSH for the All B/F/TAF Analysis....21
Table 3-7. Analysis Windows for HCV Serology and HCV RNA Assessments for the Randomized Phase Analysis....22
Table 3-8. Analysis Windows for HCV Serology and HCV RNA Assessments for the All B/F/TAF Analysis....22
Table 3-9. Analysis Windows for Safety ECG the Randomized Phase Analysis....22
Table 3-10. Analysis Windows for Safety ECG the All B/F/TAF Analysis....23

LIST OF ABBREVIATIONS

3TC	lamivudine
ABC	abacavir
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
ANOVA	analysis of variance
ARV	antiretroviral
ART	antiretroviral treatment
AST	aspartate aminotransferase
BIC	bictegravir
B/F/TAF	fixed dose combination of bictegravir (BIC; B) 50 mg / emtricitabine (FTC; F) 200 mg / tenofovir alafenamide (TAF) 25 mg
BLQ	below limit of quantitation
BMI	body mass index
CDER	Center for Drug Evaluation and Research
CG	Cockcroft-Gault
CI	confidence interval
CMH	Cochran-Mantel-Haenszel
CRF	case report form
CSR	clinical study report
CV	coefficient of variation
DC	premature study drug discontinuation
DNA	deoxyribonucleic acid
DTG	dolutegravir, tivicay
ECG	electrocardiogram
eCRF	electronic case report form
eGFR	estimated glomerular filtration rate
$eGFR_{CG}$	estimated glomerular filtration rate using Cockcroft-Gault formula
FDA	Food and Drug Administration
FDC	fixed dose combination
F/TAF	fixed dose combination of emtricitabine (FTC; F)/ tenofovir alafenamide (TAF)
FTC, F	emtricitabine
GEN	Genvoya, E/C/F/TAF
GFR	glomerular filtration rate
Gilead	Gilead Sciences, Inc.
GLPS	Global patient safety
GS-9883	bictegravir
HBcAb	hepatitis B core antibody
HBeAb	hepatitis B e-antibody
HBeAg	hepatitis B e-antigen
HBsAb	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen

HBV	hepatitis B virus
HCV	hepatitis C virus
HCVAb	hepatitis C antibody
HDL	high density lipoprotein
HIV-1	human immunodeficiency virus (Type 1)
HLGT	high level group term
HLT	high level term
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ID	identification
IDMC	independent data monitoring committee
IWRS	interactive web response system
LDL	low density lipoprotein
LLT	lowest level term
MedDRA	Medical Dictionary for Regulatory Activities
MH	Mantel-Haenszel
OL	open label
PEP	post-exposure prophylaxis
PrEP	pre-exposure prophylaxis
PK	pharmacokinetic
PP	per protocol
PT	preferred term
Q	quartile
Q1	first quartile
Q3	third quartile
QD	once daily
RBP	retinol binding protein
RNA	ribonucleic acid
SAE	serious adverse events
SAP	statistical analysis plan
SD	standard deviation
SMQ	Standardised MedDRA Query
SOC	system organ class
TAF	tenofovir alafenamide
TFL	tables, figures, and listings
TFV	tenofovir
TSH	thyroid stimulating hormone; thyrotropin
ULN	upper limit of normal
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 the final analysis clinical study report (CSR) for Study GS-US-380-1490. Final analysis will be performed when all subjects have completed the study or prematurely discontinued from the study drug. This SAP is based on the study protocol amendment 3 dated 6 May 2019 and the electronic case report form (eCRF). The SAP will be finalized before database finalization. Any changes made after the finalization of the SAP will be documented in the CSR.

1.1. Study Objectives

The primary objective of this study is:

- To evaluate the efficacy of a fixed dose combination (FDC) containing bictegravir (GS-9883; BIC; B) /emtricitabine (FTC; F) /tenofovir alafenamide (TAF) versus dolutegravir (DTG) + a FDC containing emtricitabine/tenofovir alafenamide (F/TAF) in HIV-1 infected, antiretroviral treatment (ART)-naïve adult subjects as determined by the achievement of HIV-1 ribonucleic acid (RNA) < 50 copies/mL at Week 48.

The secondary objectives of this study are:

- To evaluate the efficacy, safety, and tolerability of the 2 treatment groups through Weeks 48, 96, and 144.

- To evaluate the long-term efficacy and safety of FDC B/F/TAF through OL Weeks 48 and 96.

1.2. Study Design

Design Configuration and Subject Population

GS-US-380-1490 is a randomized, double-blinded, multicenter, active-controlled study to evaluate the safety and efficacy of B/F/TAF FDC versus DTG + F/TAF FDC in HIV-1 infected ART-naive adult subjects.

Treatment Groups

Subjects who provide written consent and meet all eligibility criteria will be randomized in a 1:1 ratio to one of the following 2 treatment groups:

Treatment Group 1: FDC of bictegravir 50 mg/ emtricitabine 200 mg/ tenofovir alafenamide 25 mg (B/F/TAF) + Placebo to match dolutegravir 50 mg and Placebo to match FDC of emtricitabine 200 mg/tenofovir alafenamide 25 mg (F/TAF) administered orally, once daily, without regard to food (n=300)

Treatment Group 2: Dolutegravir 50 mg + FDC of emtricitabine 200 mg/tenofovir alafenamide 25 mg (F/TAF) + Placebo to match FDC of bictegravir 50 mg/ emtricitabine 200 mg/ tenofovir alafenamide 25 mg (B/F/TAF) administered orally, once daily, without regard to food (n=300)

Key Eligibility Criteria

Medically stable HIV-1 infected subjects who meet the following criteria:

- Plasma HIV-1 RNA levels ≥ 500 copies/mL at screening
- ART-naive (≤ 10 days of prior therapy with any antiretroviral [ARV] agent following a diagnosis of HIV-1 infection) except the use for pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP), up to 1 month prior to screening.
- Screening genotype report must show sensitivity to FTC and tenofovir (TFV)
- Estimated GFR ≥ 30 mL/min according to the Cockcroft-Gault formula for creatinine clearance

Study Periods / Phases

Subjects will be treated for at least 144 weeks during the blinded treatment phase. After Week 144, all subjects will continue to take their blinded study drug and attend visits every 12 weeks until the End of Blinded Treatment Visit. Once the last subject completes the Week 144 visit and Gilead Sciences Inc. (Gilead) completes the Week 144 analysis, all subjects will return to the clinic (preferably within 30 days) for an End of Blinded Treatment Visit. At the End of Blinded Treatment Visit, subjects will be given the option to receive B/F/TAF FDC in an open-label (OL) extension phase for 96 weeks. After Week 96 OL, subjects will discontinue the study drug, transition onto commercially available treatment and complete a 30-Day Follow-up Visit. In a country where B/F/TAF is not available, subjects will be given the option to continue OL B/F/TAF until the product becomes accessible to subjects through an access program, or until Gilead elects to discontinue the study in that country, whichever occurs first.

All subjects participating in the OL extension phase, without regard to their blinded treatment regimen, will return for study visits at Week 12 OL and every 12 weeks thereafter for 96 weeks.

Subjects who complete the study through the End of Blinded Treatment Visit and do not continue on the OL B/F/TAF FDC extension phase will be required to return to the clinic after the End of Blinded Treatment Visit for a 30-Day Follow-Up Visit.

Treatment assignments will be provided to the investigators within 30 days of the last subject completing the End of Blinded Treatment Visit.

Schedule of Assessments

After screening procedures, eligible subjects will be randomized 1:1 to Treatment Group 1 or Treatment Group 2 and treated for 144 weeks. Following the Day 1 visit, subjects will be required to return for study visits at Weeks 4, 8, and 12, and then every 12 weeks from Week 12 through Week 144. After Week 144, all subjects will continue to take their blinded study drugs and attend study visits every 12 weeks until the End of Blinded Treatment Visit. All subjects participating in the OL extension phase, without regard to their blinded treatment regimen, will return for study visits at Week 12 OL and every 12 weeks thereafter for at least 96 weeks.

For all eligible subjects, blood will be collected at Day 1, Weeks 4, 8, 12, and then every 12 weeks through the End of Blinded Treatment Visit. Blood will also be collected at Week 12 OL and every 12 weeks thereafter for at least 96 weeks during the OL extension phase. Laboratory analyses (hematology, chemistry, and urinalysis), HIV-1 RNA, CD4+ cell count, and complete or symptom-directed physical examinations will be performed at Screening, Day 1, and all subsequent visits.

Adverse events (AEs) and concomitant medications will be assessed at each visit.

More details for study procedures can be found in Appendix 1.

Pharmacokinetics

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For all subjects on study drug, a single anytime pre- or post-dose PK blood sample will be collected at Weeks 8, 24, and 36.

For all subjects on study drug, a trough PK blood sample will be obtained 20-28 hours following the last dose at Weeks 4 and 12. Following an observed dose, one post-dose PK blood sample will be collected between 1 and 4 hours post-dose.

Randomization

Subjects will be randomized in a 1:1 ratio to 1 of 2 Treatment Groups (Treatment Group 1: Treatment Group 2). Randomization will be stratified by HIV-1 RNA level ($\leq$ 100,000 copies/mL, > 100,000 to $\leq$ 400,000 copies/mL, or > 400,000 copies/mL) at screening, CD4+ cell count (< 50 cells/µL, 50 – 199 cells/µL, or $\geq$ 200 cells/µL) at screening, and region (US or Ex-US) at randomization.

Site and/or Stratum Enrollment Limits

Approximately 150 study sites in North America, Europe, and Latin America participated. There was no enrollment limit for individual sites.

Study Duration

The randomized, double-blind phase of this study is at least 144 weeks in duration. The OL phase is 96 weeks duration.

1.3. Sample Size and Power

A total of approximately 600 HIV-1 infected subjects, randomized in a 1:1 ratio to 2 treatment groups (300 subjects per treatment group), achieves at least 95% power to detect a noninferiority margin of 12% in Week 48 response rate (HIV-1 RNA < 50 copies/mL as determined by the United States [US] Food and Drug Administration [FDA]-defined snapshot algorithm) difference between the 2 treatment groups. For sample size and power computation, it is assumed that both treatment groups have a response rate of 91% (based on Gilead Genvoya [GEN; E/C/F/TAF] Studies GS-US-292-0104 and GS-US-292-0111), that a noninferiority margin is 12%, and that the significance level of the test is at a one-sided 0.025 level. Sample size and power calculations were made using the statistical software package nQuery Advisor (Version 6.0).

2. TYPE OF PLANNED ANALYSIS

2.1. Data Monitoring Committee Analyses

The Week 12 Independent Data Monitoring Committee (IDMC) analysis was conducted after approximately the first 50% of subjects enrolled completed their Week 12 visit or prematurely discontinued the study drug. The Week 24 IDMC analysis was conducted after all subjects enrolled completed their Week 24 visit or prematurely discontinued the study drug. The purpose of these interim analyses was to provide the IDMC with a statistical report for review. More details are documented in the IDMC charter.

Gilead does not have a prior intent to ask the IDMC to review Week 48 results or to consider early termination of the study even if there is early evidence of favorable efficacy for B/F/TAF.

2.2. Interim Analyses

2.2.1. Week 48 Analysis

The Week 48 analysis was conducted after all subjects either completed their Week 48 visit or prematurely discontinued from the study drug.

2.2.2. Week 96 Analysis

The Week 96 analysis was conducted after all subjects either completed their Week 96 visit or prematurely discontinued from the study drug.

2.2.3. Week 144 Analysis

The Week 144 analysis was conducted after all subjects either complete their Week 144 visit or prematurely discontinue from the study drug.

2.2.4. Open Label Week 48 Analysis

The OL Week 48 analysis was conducted after all subjects either complete their open label Week 48 visit or prematurely discontinue from the study drug.

2.3. Final Analysis

The final statistical analysis will be conducted after all subjects either complete the study or prematurely discontinue from the study.

This statistical analysis plan describes the analysis plan for the final analysis.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

The Final Analysis will include two sets of analysis: randomized phase analysis and all B/F/TAF analysis. All table summaries in this final analysis will be based on data included in the All B/F/TAF analysis (eg, data collected during the study period when participants were on B/F/TAF). Randomized phase analysis (eg, including data collected during double-blind phase when participants were on the double-blind study drug) and the corresponding analysis window defined in Section 3.8, will be used to support applicable listings where data collected from the double-blind phase are indicated. The wording of randomized phase or double-blind phase might be used interchangeably throughout the SAP and in the TFLs.

Randomized Phase Analysis:

- For subjects who are never treated in the extension phase of the study including those who prematurely discontinue the randomized study drug or who complete the randomized study drug and do not receive any dose of B/F/TAF in the extension phase, all available data will be included in the randomized phase analysis.

- For subjects who complete the randomized phase and receive at least 1 dose of B/F/TAF in the extension phase, the randomized phase analysis will include (1) all available AE, concomitant medication, pregnancy, and death data collected prior to the extension phase first dose date; (2) all available other data, such as laboratory, vital sign, electrocardiogram (ECG), collected on or prior to the extension phase first dose date.

All B/F/TAF Analysis:

- For subjects who receive B/F/TAF in the randomized phase, all available data for subjects who actually receive B/F/TAF in the randomized phase will be included.

- For subjects who actually receive DTG+F/TAF in the randomized phase and receive at least 1 dose of B/F/TAF in the extension phase, (1) all available AE, concomitant medication, pregnancy, and death data with start date **on or after** the first dose date of B/F/TAF in the extension phase and (2) all available other data, such as laboratory, vital sign, and ECG data, collected **after** the first dose date of B/F/TAF in the extension phase will be included. The data collected **on or prior to** the first dose date of B/F/TAF will be used to derive the baseline value for the all B/F/TAF analysis.

Note that all data for subjects who actually receive DTG+F/TAF in the randomized phase and do not receive any dose of B/F/TAF in the extension phase will be excluded from all B/F/TAF analysis. The actual treatment received will differ from the randomized treatment only when the actual treatment received differs from randomized treatment for the entire treatment duration.

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.

All statistical tests will be 2-sided and performed at the 5% significance level unless otherwise specified.

For All B/F/TAF analysis, no statistical comparison between treatment groups will be conducted.

By-subject listings will be presented for all subjects in the All Randomized Analysis Set unless otherwise specified, and sorted by subject ID number, visit date, and time (if applicable). Data collected on log forms, such as AEs, will be presented in chronological order within a subject. The treatment group to which subjects were randomized will be used in the listings. Most listings will be provided for all randomized analysis set for data from both phases of the study. Some listings for All B/F/TAF analysis set will also be provided.

In general, age (in years) on the date of the first dose of study drug will be used for analyses and presentation in listings. For randomized but never dosed subjects, age on the date of randomization will be used. For screen failures, age on the date of the informed consent was signed will be used. If only birth year is collected on the eCRF, “01 January” will be used for the unknown birth day and month for the purpose of age calculation, similarly, if only birth year and month are collected on the eCRF, “01” will be used for the unknown birth day for the purpose of age calculation.

In general, permanent discontinuation of the randomized study drug refers to premature discontinuation of the randomized study drug or completion of the randomized study drug. Similarly, permanent discontinuation of the extension phase study drug refers to premature discontinuation of the extension phase study drug or completion of the extension phase study drug. More specifically, for randomized phase analysis, study drug refers to the randomized study drugs (B/F/TAF or DTG+F/TAF); for all B/F/TAF analysis, study drug refers to B/F/TAF.

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 included as a subtitle of each table, figure, and listing. A summary of the number and percentage of subjects in each Analysis Set will be provided by treatment group and in total.

3.1.1. All Randomized Analysis Set

The **All Randomized Analysis Set** will include all subjects who are randomized into the two arms of the study. This is the primary analysis set for by-subject listings.

3.1.2. All B/F/TAF Analysis Set

The **All B/F/TAF Analysis Set** will include all subjects who (1) are randomized into the study and (2) have received at least 1 dose of the B/F/TAF in the randomized phase or at least 1 dose of the B/F/TAF in the extension phase. This is the primary analysis set for the all B/F/TAF efficacy and safety analyses.

For efficacy analyses, all efficacy data collected for the all B/F/TAF analysis will be included.

For safety analyses, all safety data collected up to 30 days after permanent discontinuation of the B/F/TAF (including randomized and open label phases) will be included in the safety summaries, unless specified otherwise.

3.2. Subject Grouping

For analysis using the All Randomized Analysis Set, subjects will be grouped by the randomized treatment (labeled as B/F/TAF vs. DTG/F/TAF).

For all analyses included in the all B/F/TAF analysis, subjects will be grouped into the following 2 groups:

- B/F/TAF group: This group includes all subjects who actually received B/F/TAF in the randomized phase of this study, regardless whether subjects receive any B/F/TAF in the extension phase or not.

- DTG/F/TAF to B/F/TAF group: This group includes all subjects who actually received DTG+F/TAF regimen in the randomized phase of this study and then receive at least 1 dose of B/F/TAF in the extension phase.

3.3. Strata and Covariates

Randomization was stratified by HIV-1 RNA level (≤ 100,000 copies/mL, > 100,000 copies/mL to ≤ 400,000 copies/mL, or > 400,000 copies/mL) at screening, CD4+ cell count (< 50 cells/μL, 50 - 199 cells/μL, or ≥ 200 cells/μL) at screening, and region (US or Ex-US) at randomization.

3.4. Examination of Subject Subgroups

3.4.1. Subject Subgroups for Safety Analyses

Selected safety endpoints may be analyzed for the following subject subgroups (see Section 9.1 for details) for all B/F/TAF analysis set:

- Subjects with HIV/HBV coinfection at baseline

- Subjects with incident HIV/HBV coinfection while on study drug (if any)

Selected safety endpoints will be analyzed for the following subject subgroups (see Section 9.2 for details):

- Subjects with HIV/hepatitis C virus (HCV) coinfection at baseline
- Subjects with incident HIV/HCV coinfection while on study drug (if any)

3.5. Multiple Comparisons

No alpha level adjustment is applied other than for the primary endpoint.

3.6. Missing Data and Outliers

3.6.1. Missing Data

A missing datum for a given study analysis window may be due to any of the following reasons:

- A visit occurring in the window but data were not collected or were unusable
- A visit not occurring in the window
- A subject prematurely discontinuing from the study before reaching the window

In general, values for missing data will not be imputed, unless methods for handling missing data are specified.

For missing last dosing date of study drug, imputation rules are described in Section 3.8.1. The handling of missing or incomplete dates for AE onset is described in Section 7.1.5.2, and for concomitant medications in Section 7.4.2.

3.6.2. Outliers

Outliers will be identified during the data management and data analysis process, but no sensitivity analyses will be done to evaluate the impact of outliers on efficacy or safety outcomes, unless specified otherwise. All data will be included in the analyses.

3.7. Data Handling Conventions and Transformations

Laboratory data that are continuous in nature but are less than the lower limit of quantitation or above the upper limit of quantitation will be imputed as follows except for urine creatinine:

- A value that is 1 unit less than the limit of quantitation will be used for calculation of descriptive statistics if the datum is reported in the form of "< x" (where x is considered the limit of quantitation). For example, if the values are reported as < 50 and < 5.0, values of 49 and 4.9, respectively, will be used for calculation of 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 for calculation of summary statistics.

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

- The limit of quantitation will be used for calculation of descriptive statistics if the datum is reported in the form of "≤ x" or "≥ x" (where x is considered the limit of quantitation).

For urine creatinine, a value of "< 1" is handled as a missing value in its summary and the calculation of related ratios.

Logarithmic (base 10) transformations will be applied to HIV-1 RNA and HBV DNA data for efficacy analyses. HIV-1 RNA results of "No HIV-1 RNA detected" and "<20 cp/mL HIV-1 RNA Detected" will be imputed as 19 copies/mL for analysis purposes. HBV DNA results of "<20 IU/mL HBV DNA detected" or "No HBV DNA detected" will be imputed as 19 IU/mL for analysis purposes. HCV RNA results of "<15 IU/mL HCV RNA detected" or "No HCV RNA detected" will be imputed as 14 IU/mL for analysis purposes.

3.8. Analysis Windows

3.8.1. Definition of Study Day

Study Day 1 for the Randomized Phase analysis is defined as the day when the first dose of study drug (ie, B/F/TAF, DTG /F/TAF) was taken, as recorded on "Randomized Phase" the Study Drug Administration eCRF form.

Last Dose Date for the Randomized Phase analysis is the latest of the randomized study drug (including B/F/TAF or DTG/F/TAF) end dates recorded on the Study Drug Administration eCRF form.

If last dose date for the Randomized Phase analysis is missing (eg, only year of last dose date is known or completely missing due to lost to follow-up), the latest of the randomized study drug start dates and end dates or the latest clinical and laboratory visit dates prior to the first dose date of B/F/TAF in the extension phase (if applicable), excluding the 30-day follow-up visit date, will be used to impute the last dose date. For other partial missing last dose date, please see the programming specifications for imputation rule details.

Study Day 1 for the all B/F/TAF analysis is defined as

- For subjects who actually received B/F/TAF in the randomized phase of this study (ie, B/F/TAF group), Study Day 1 for the all B/F/TAF analysis is defined as the day when the first dose of B/F/TAF in the randomized phase was taken, as recorded on the Study Drug Administration eCRF form.

- For subjects who actually received DTG/F/TAF in the randomized phase of this study and then receive at least 1 dose of B/F/TAF in the extension phase (ie, DTG/F/TAF to B/F/TAF group), Study Day 1 for the all B/F/TAF analysis is defined as the day when the first dose of B/F/TAF in the extension phase was taken, as recorded on the Study Drug Administration eCRF form.

Last Dose Date for the All B/F/TAF Analysis is the latest of B/F/TAF (including both phases) end dates recorded on the Study Drug Administration eCRF form.

If the last dose date for the all B/F/TAF analysis is missing (eg, only year of last dose date is known or completely missing due to lost to follow-up), the latest of the B/F/TAF (including both phases) start dates and end dates, the latest clinical and laboratory visit dates, excluding the 30-day follow-up visit date, will be used to impute the last dose date.

Study Days are calculated relative to Study Day 1 for either the randomized phase analysis or the all B/F/TAF analysis, as appropriate. For events that occurred on or after the Study Day 1 date of either analysis, study days are calculated as (visit date minus the date of Study Day 1 plus 1). For events that occurred prior to Study Day 1 for either analysis, study days are calculated as (visit date minus the date of Study Day 1).

Last Study Date is the latest of the study drug (including B/F/TAF and DTG/F/TAF in both phases) start dates and end dates, the clinic visit dates, and the laboratory visit dates, including the 30-day follow-up visit date.

Baseline Value is defined as the last nonmissing value obtained on or prior to Study Day 1 for either the randomized phase analysis or the all B/F/TAF analysis, as appropriate. Subjects who actually received DTG+F/TAF in the randomized phase and received at least 1 dose of B/F/TAF in extension phase will have a new baseline value for the All B/F/TAF analysis.

3.8.2. Analysis Windows

Subject visits might not occur on protocol-specified days. Therefore, for the purpose of analysis, observations will be assigned to two different sets of analysis windows based on the following tables: the analysis windows for the randomized phase analysis are derived relative the Study Day 1 for the randomized phase analysis, while the analysis windows for the all B/F/TAF analysis are derived relative the Study Day 1 for the all B/F/TAF analysis.

The analysis windows for HIV-1 RNA, CD4+ cell count, CD4 %, hematology, chemistry, urinalysis, urine pregnancy laboratory tests, $eGFR_{CG}$, vital signs, and weight (if collected) are presented in Table 3-1 and Table 3-2 for the randomized phase analysis and the All B/F/TAF analysis separately.

Table 3-1. Analysis Windows for HIV-1 RNA, CD4+ cell count, CD4 %, HBV DNA, Hematology, Chemistry, Urinalysis, Urine Pregnancy Laboratory Tests, $eGFR_{CG}$, Vital Signs, and Weight for the Randomized Phase Analysis

Visit ID	Nominal Day	Lower Limit	Upper Limit
Baseline			1
Week 4	28	2	42
Week 8	56	43	70
Week 12	84	71	126
Week 24	168	127	210
Week 36	252	211	294
Week 48	336	295	378
Week 60	420	379	462
Week 72	504	463	546
Week 84	588	547	630
Week 96	672	631	714
Week 108	756	715	798
Week 120	840	799	882
Week 132	924	883	966
Week 144	1008	967	1050
Week K (K is every 12 weeks after previous visit)	K*7	(K-6)*7+1	(K+6)*7

Table 3-2. Analysis Windows for HIV-1 RNA, CD4+ cell count, CD4 %, HBV DNA, Hematology, Chemistry, Urinalysis, and Urine Pregnancy Laboratory Tests, $eGFR_{CG}$, Vital Signs, and Weight for the All B/F/TAF Analysis

	B/F/TAF Group			DTG/F/TAF to B/F/TAF		
Visit ID	**Nominal Day**	**Lower Limit**	**Upper Limit**	**Nominal Day**	**Lower Limit**	**Upper Limit**
Baseline			1			1
Week 4	28	2	42	NA	NA	NA
Week 8	56	43	70	NA	NA	NA
Week 12	84	71	126	84	2	126
Week 24	168	127	210	168	127	210
Week 36	252	211	294	252	211	294
Week 48	336	295	378	336	295	378
Week 60	420	379	462	420	379	462
Week 72	504	463	546	504	463	546
Week 84	588	547	630	588	547	630
Week 96	672	631	714	672	631	714
Week k	K*7	(K-6)*7+1	(K+6)*7	K*7	(K-6)*7+1	(K+6)*7

NA = Not applicable
Note: For the B/F/TAF group, Study Day 1 is the first dose date of the B/F/TAF received in the randomized phase;
Note: For the DTG/F/TAF to B/F/TAF group, Study Day 1 is the first dose date of the B/F/TAF received in the extension phase.
Note: Week k is every 12 weeks after previous visit.

The analysis windows for metabolic assessments (including fasting glucose and lipid panel: total cholesterol, high density lipoprotein [HDL], direct low density lipoprotein [LDL], triglycerides, and total cholesterol to HDL ratio) and HBV serology (including hepatitis B surface antibody [HBsAb], hepatitis B surface antigen [HBsAg], hepatitis B e-antigen [HBeAg], and reflex hepatitis B e-antibody [HBeAb] if HBeAg is negative, for subjects who are HBV infected at any visit and HBsAb, HBcAb, HBsAg, for those subjects who do not meet the definition of HBV infection at any visit) are presented in Table 3-3 and Table 3-4. Note: HBV serology is only collected at Baseline, Week 48, and every 48 weeks for subjects who are not HBV infected at any visit.

Table 3-3. Analysis Windows for Metabolic Assessments and HBV Serology for the Randomized Phase Analysis

Visit ID	Nominal Day	Lower Limit	Upper Limit
Baseline			1
Week 12	84	2	126
Week 24	168	127	252
Week 48	336	253	420
Week 72	504	421	588
Week 96	672	589	756
Week 120	840	757	924
Week 144	1008	925	1092
Week K (K is every 24 weeks after previous visit)	K*7	(K-12)*7+1	(K+12)*7

Table 3-4. Analysis Windows for Metabolic Assessments and HBV Serology for the All B/F/TAF Analysis

	B/F/TAF Group			DTG/F/TAG to B/F/TAF		
Visit ID	Nominal Day	Lower Limit	Upper Limit	Nominal Day	Lower Limit	Upper Limit
Baseline			1			1
Week 12	84	2	126	NA	NA	NA
Week 24	168	127	252	168	2	252
Week 48	336	253	420	336	253	420
Week 72	504	421	588	504	421	588
Week 96	672	589	756	672	589	756
Week K	K*7	(K-12)*7+1	(K+12)*7	K*7	(K-12)*7+1	(K+12)*7

NA = Not applicable
Note: For the B/F/TAF group, Study Day 1 is the first dose date of the B/F/TAF received in the randomized phase;
Note: For the DTG/F/TAF to B/F/TAF group, Study Day 1 is the first dose date of the B/F/TAF received in the extension phase.
Note: Week k is every 24 weeks after previous visit.

The analysis windows for thyroid stimulating hormone (TSH; thyrotropin) are presented in Table 3-5 for the Randomized Phase Analysis and Table 3-6 for the All B/F/TAF Analysis.

Table 3-5. Analysis Windows for TSH for the Randomized Phase Analysis

Visit ID	Nominal Day	Lower Limit	Upper Limit
Baseline			1
Week 24	168	2	252
Week 48	336	253	420
Week 72	504	421	588
Week 96	672	589	756
Week 120	840	757	924
Week 144	1008	925	1092
Week K (K is every 24 weeks after previous visit)	K*7	(K-12)*7+1	(K+12)*7

Table 3-6. Analysis Windows for TSH for the All B/F/TAF Analysis

	B/F/TAF Group			DTG/F/TAF to B/F/TAF		
Visit ID	Nominal Day	Lower Limit	Upper Limit	Nominal Day	Lower Limit	Upper Limit
Baseline			1			1
Week 24	168	2	252	168	2	252
Week 48	336	253	420	336	253	420
Week 72	504	421	588	504	421	588
Week 96	672	589	756	672	589	756
Week k	K*7	(K-12)*7+1	(K+12)*7	K*7	(K-12)*7+1	(K+12)*7

NA = Not applicable
Note: For the B/F/TAF group, Study Day 1 is the first dose date of the B/F/TAF received in the randomized phase;
Note: For the DTG/F/TAF to B/F/TAF group, Study Day 1 is the first dose date of the B/F/TAF received in the extension phase.
Note: Week k is every 24 weeks after previous visit.

The analysis windows for HCV serology (HCV antibody [HCVAb]) and HCV RNA assessments are presented in Table 3-7 for the Randomized Phase Analysis and Table 3-8 for the All B/F/TAF Analysis.

Table 3-7. Analysis Windows for HCV Serology and HCV RNA Assessments for the Randomized Phase Analysis

Visit ID	Nominal Day	Lower Limit	Upper Limit
Baseline			1
Week 48	336	2	504
Week 96	672	505	840
Week 144	1008	841	1176
Week K (K is every 48 weeks after previous visit)	K*7	(K-24)*7+1	(K+24)*7

Table 3-8. Analysis Windows for HCV Serology and HCV RNA Assessments for the All B/F/TAF Analysis

	B/F/TAF Group			DTG+F/TAF to B/F/TAF		
Visit ID	Nominal Day	Lower Limit	Upper Limit	Nominal Day	Lower Limit	Upper Limit
Baseline			1			1
Week 48	336	2	504	336	2	504
Week 96	672	505	840	672	505	840
Week k	K*7	(K-24)*7+1	(K+24)*7	K*7	(K-24)*7+1	(K+24)*7

NA = Not applicable
Note: For the B/F/TAF group, Study Day 1 is the first dose date of the B/F/TAF received in the randomized phase;
Note: For the DTG/F/TAF to B/F/TAF group, Study Day 1 is the first dose date of the B/F/TAF received in the extension phase.
Note: Week k is every 48 weeks after previous visit.

The analysis windows for safety electrocardiogram (ECG) are presented in Table 3-9 for the Randomized Phase Analysis, and Table 3-10 for the All B/F/TAF Analysis.

Table 3-9. Analysis Windows for Safety ECG the Randomized Phase Analysis

Visit ID	Nominal Day	Lower Limit	Upper Limit
Baseline			1
Week 24	168	2	252
Week 48	336	253	504
Week 96	672	505	840
Week 144	1008	841	1176
Week K (K is every 48 weeks after previous visit)	K*7	(K-24)*7+1	(K+24)*7

Table 3-10. Analysis Windows for Safety ECG the All B/F/TAF Analysis

	B/F/TAF Group			DTG+F/TAF to B/F/TAF		
Visit ID	Nominal Day	Lower Limit	Upper Limit	Nominal Day	Lower Limit	Upper Limit
Baseline			1			1
Week 24	168	2	252	NA	NA	NA
Week 48	336	253	504	336	2	504
Week 96	672	505	840	672	505	840
Week k	K*7	(K-24)*7+1	(K+24)*7	K*7	(K-24)*7+1	(K+24)*7

Note: For the B/F/TAF group, Study Day 1 is the first dose date of the B/F/TAF received in the randomized phase;
Note: For the DTG/F/TAF to B/F/TAF group, Study Day 1 is the first dose date of the B/F/TAF received in the extension phase.
Note: Week k is every 48 weeks after previous visit.
NA=Not Applicable.

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

Depending on the statistical analysis method, single values are 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 one value per analysis window. When a single value is needed, the following rule(s) will be used.

If multiple nonmissing numeric observations exist in a window, then records will be chosen as follows:

- For baseline, the latest available record on or prior to the first dose date of study drug will be selected. If there are multiple records with the same time or no time recorded on the same day, average will be used for the baseline value, except for HIV-1 RNA (see below).
- For postbaseline visits:
  - For CD4+ cell count, CD4%, and HBV DNA, the record(s) collected on the latest day in the window will be selected for analysis.
  - For other numeric observations (ie, except HIV-1 RNA, CD4+ cell count, CD4%, and HBV DNA), the record(s) collected on the day closest to the nominal day for that visit will be selected. If there are 2 days equidistant from the nominal day, the later day will be selected.
  - For any numeric observations except HIV-1 RNA, if there are multiple records on the selected day, the average will be taken.
- For baseline and postbaseline HIV-1 RNA, the latest (considering both date and time) record(s) in the window will be selected. If both “HIV RNA Taqman 2.0” and “HIV RNA Repeat” (ie, the HIV-1 RNA result obtained from an additional aliquot of the original sample) are available with the same collection time, the results from the “HIV RNA Repeat” will be selected for analysis purposes; otherwise, if there are multiple “HIV RNA Taqman 2.0” records with the same collection time, the geometric mean will be taken for analysis purposes.

If multiple valid nonmissing categorical observations exist in a window, records will be chosen as follows:

- For baseline, the last available record on or prior to the first dose date of study drug will be selected. If there are multiple records with the same time or no time recorded on the same day, the value with the lowest severity will be selected (eg, normal will be selected over abnormal for safety ECG findings).

- For postbaseline visits, the most conservative value within the window will be selected (eg, abnormal will be selected over normal for safety ECG findings).

4. SUBJECT DISPOSITION

4.1. Subject Enrollment and Disposition

4.1.1. Subject Enrollment

All necessary summaries on subject enrollment have been performed as part of the Week 48 CSR, and will not be repeated for the final analysis.

4.1.2. Subject Disposition

The summary of subject disposition will be provided by treatment group and overall for all randomized subjects. This summary will include subjects randomized, subjects randomized but never treated, subjects in the Safety Analysis Set, and subjects in the FAS.

In addition, the number and percentage of the subjects in the following categories will be summarized:

- Subjects completing study drug in the randomized phase
- Subjects prematurely discontinuing study drug in the randomized phase (with summary of reasons for discontinuing study drug in the randomized phase)
- Subjects completing study in the randomized phase
- Subjects prematurely discontinuing from study in the randomized phase (with summary of reasons for discontinuing from study in the randomized phase)
- Subjects entering the OL extension phase
- Subjects treated in the OL extension phase
- Subjects completing study drug in the OL extension phase
- Prematurely discontinuing study drug in the OL extension phase (with summary of reasons for discontinuing study drug in the OL extension phase)
- Subjects completing study in the OL extension phase
- Prematurely discontinuing from study in the OL extension phase (with summary of reasons for discontinuing from study in the OL extension phase)

The denominator for the percentages of subjects in each category in the randomized phase, including "Subjects entering the OL extension phase", will be the number of subjects randomized and treated in the randomized phase. The denominator for the percentages of subjects in each category in the OL extension phase will be the number of subjects who were treated in OL extension phase.

No inferential statistics will be generated. A data listing of reasons for premature study drug/study discontinuation will be provided. Reasons for premature study drug/study discontinuation due to COVID-19 will also be provided in a separate listing.

4.2. Extent of Study Drug Exposure and Adherence

4.2.1. Duration of Exposure to Study Drug

Duration of exposure to study drug will be defined for the all B/F/TAF analysis. For the all B/F/TAF analysis, the terms "first dose date" and "last dose date" in the text below refer to the first dose date and last dose date defined for the all B/F/TAF phase analysis. Duration of exposure to study drug will be defined as (the last dose date – the first dose date + 1), regardless of temporary interruptions in study drug administration, and will be expressed in weeks using up to 1 decimal place (eg, 4.5 weeks).

Duration of exposure to study drug will be summarized using descriptive statistics (sample size, mean, SD, median, Q1, Q3, minimum, and maximum) and as the number and percentage of subjects exposed for specified periods, eg, ≥ 4 weeks (28 days), ≥ 8 weeks (56 days), ≥ 12 weeks (84 days), ≥ 24 weeks (168 days), ≥ 36 weeks (252 days), ≥ 48 weeks (336 days), ≥ 60 weeks (420 days), ≥ 72 weeks (504 days), ≥ 84 weeks (588 days), ≥ 96 weeks (672 days), ≥ 108 weeks (756 days), ≥ 120 weeks (840 days), ≥ 132 weeks (924 days), ≥ 144 weeks (1008 days), etc.

Summaries will be provided by treatment group for subjects in All B/F/TAF Analysis Set for the all B/F/TAF analysis, respectively. No inferential statistics will be provided.

Time to premature discontinuation of study drug will be analyzed by treatment group using the Kaplan-Meier (KM) method for the All B/F/TAF Analysis Set. No statistical comparisons will be made for the all B/F/TAF analysis. A plot of KM estimates for the time to premature discontinuation of study drug by treatment group will be generated for the All B/F/TAF analysis. Subjects who completed study drug will be censored at the last dose data of the study.

4.2.2. Adherence to Study Drug Regimen

Adherence to study drug regimen will be defined for the all B/F/TAF analysis. For all B/F/TAF analysis, study drug adherence (for B/F/TAF) will be computed for both treatment groups as defined in Section 3.2. Study drug regimen adherence will be computed based on pill counts. The numbers of pills of study drug dispensed and returned are captured on study drug accountability eCRF.

Adherence (%) of study drug regimen will be calculated as follows:

$$\text{Adherence}(\%) = 100 \times \frac{\text{Total No. of pills taken}}{\text{Total No. of pills prescribed}}$$

$$= 100 \times \frac{\sum \text{No. of pills taken at each dispensing period}^{[1]}}{\sum \text{No. of pills prescribed at each dispensing period}^{[2]}}$$

[1] Number of pills taken at a distinct dispensing period for a study drug is calculated as the minimum of (a) the daily number of pills prescribed for the study drug multiplied by the duration of treatment at the dispensing period, and (b) the number of pills taken for the study drug (number of pills dispensed minus the number of pills returned). Total number of pills taken is determined by summing the number of pills taken from all evaluable dispensing periods.

[2] Number of pills prescribed at a distinct dispensing period for a study drug is calculated as the daily number of pills prescribed for the study drug multiplied by the duration of treatment at the dispensing period. Total number of pills prescribed is determined by summing the number of pills prescribed from all evaluable dispensing periods.

The duration of treatment at a dispensing period for a study drug is calculated as the minimum of (a) the last returned date of study drug at a dispensing period, (b) date of premature discontinuation of the study drug, and (c) next pill dispensing date of the study drug, minus dispensing date of the study drug.

The next pill dispensing date is the following dispensing date of the study drug regardless of the bottle return date.

For a record where the number of pills returned was missing (with "Yes" answered for "Was Bottle returned?" question), it is assumed the number of pills returned was zero. If the number of pills dispensed was missing or any study drug bottle was not returned or the bottle return status was unknown, then all records in that dispensing period for that study drug will be excluded from both denominator and numerator calculation.

Overall adherence will be calculated for the all B/F/TAF analysis. Overall adherence for the all B/F/TAF analysis will use all available data for subjects who actually received B/F/TAF in the randomized phase, and data on or after the first dose date of extension B/F/TAF for subjects who actually received DTG+F/TAF in the randomized phase and received at least 1 dose of B/F/TAF in the extension phase.

Descriptive statistics for adherence to a study drug regimen (sample size, mean, SD, median, Q1, Q3, minimum, and maximum) along with the number and percentage of subjects belonging to adherence categories (eg, $< 80\%$, $\geq 80\%$ to $< 90\%$, $\geq 90\%$ to $< 95\%$, $\geq 95\%$) will be provided by treatment group for subjects who return at least 1 bottle of randomized study drug, and who have calculable adherence for the All B/F/TAF Analysis Set. No inferential statistics will be provided.

4.3. Protocol Deviations

A listing will be provided for all randomized subjects who violated at least 1 inclusion or exclusion criterion. The listing will include the criteria not met. A listing of subjects who received the wrong study drug will also be provided.

4.4. Missing Protocol-Specified Information due to COVID-19

An overall summary of the number and percentage of subjects with missed or virtual visits (e.g., at least 1, with 1, 2, 3 or more visits) due to the COVID-19 pandemic will be provided. The denominator for the percentage calculation will be the total number of subjects in the all B/F/TAF analysis set.

A by-subject listing of subjects with missed or virtual visits due to COVID-19 will be provided by subject ID number in ascending order.

The determination of missing or virtual Visits due to COVID-19 was done using Natural Language Processing (NLP) to search the CRF comment fields. A detailed explanation of the algorithm is given in Appendix 5.

5. BASELINE CHARACTERISTICS

5.1. Demographics and Baseline Characteristics

Subject demographic data (eg, age, sex at birth, race, and ethnicity) and baseline characteristics (eg, body weight, height, and body mass index [BMI]) will be summarized by treatment group and overall using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) for continuous data and by the number and percentage of subjects for categorical data. The summaries of demographic data and baseline characteristics will be provided by treatment groups for subjects in the All B/F/TAF Analysis Set (noticing that the baseline for all B/F/TAF analysis will be adjusted based on first dose of B/F/TAF), respectively.

No statistical comparisons will be made for the All B/F/TAF analysis.

5.2. Baseline Disease Characteristics

The following baseline disease characteristics will be summarized by treatment group and overall using descriptive statistics for subjects in All B/F/TAF A:

- HIV-1 RNA (log_{10} copies/mL)
- HIV-1 RNA categories (copies/mL): (a) ≤ 100,000, (b) > 100,000 to ≤ 400,000, and (c) > 400,000
- CD4+ cell count (/μL)
- CD4+ cell count categories (/μL): (a) < 50, (b) ≥ 50 to < 200, (c) ≥ 200 to < 350, (d) ≥ 350 to < 500, and (e) ≥ 500
- CD4 percentage (%)
- Mode of infection (HIV risk factors)
- HIV disease status
- $eGFR_{CG}$ (mL/min)
- HIV/HBV coinfection status (Yes/No/Missing, see Section 9.1 for definition)
- HIV/HCV coinfection status (Yes/No/Missing, see Section 9.2 for definition)

No statistical comparisons will be made for the all B/F/TAF analysis.

5.3. Medical History

General medical history data will be collected at screening and listed only. General medical history data will be coded using the current version of Medical Dictionary for Regulatory Activities (MedDRA).

6. EFFICACY ANALYSES

All necessary summaries on the primary efficacy endpoint (at Week 48) and the secondary endpoints at Weeks 48, 96 and 144 have been performed as part of the Week 48 CSR, Week 96 CSR, Week 144 CSR and will not be repeated for the final analysis.

6.1. Primary Efficacy Endpoint

The primary efficacy endpoint is the proportion of subjects with HIV-1 RNA < 50 copies/mL at Week 48 as determined by the US FDA-defined snapshot algorithm {U. S. Department of Health and Human Services 2015}. The proportions are expressed as percentages for presentation purposes.

The statistical analysis methods for the primary efficacy endpoint were described in the Week 48 SAP and the analysis was performed in the Week 48 analysis.

6.2. Secondary Efficacy Endpoints

6.2.1. Definition of the Secondary Efficacy Endpoints

The secondary efficacy endpoints include:

- The proportion of subjects with HIV-1 RNA < 50 copies/mL at Weeks 96 and 144 as determined by the US FDA-defined snapshot algorithm
- The proportion of subjects with HIV-1 RNA < 20 copies/mL at Weeks 48, 96, and 144 as determined by the US FDA-defined snapshot algorithm
- The change from baseline in $\log_{10}$ HIV-1 RNA and CD4+ cell count at Weeks 48, 96, and 144
- The proportion of subjects who achieve HIV-1 RNA < 50 copies/mL at OL Week 48 and OL Week 96 as defined by Missing = Excluded and Missing = Failure algorithm
- The change from baseline in CD4+ cell count at OL Weeks 48 and 96.

The statistical analysis methods for the secondary efficacy endpoints at Weeks 48, 96, and 144 (based on data included in the randomized phase analysis)and at Week 48 OL (based on data included in the All B/F/TAF analysis) were described in the previous interim analyses SAPs or programming specification, and the analyses were performed in the previous interim analyses. In this final analysis, the last 2 secondary endpoints will be analyzed for all visits with details defined in the next section (Section 6.3).

6.3. Efficacy Endpoints for all B/F/TAF Analysis

6.3.1. Definition of the Efficacy Endpoint for all B/F/TAF analysis

The efficacy endpoints for all B/F/TAF analysis include:

- The proportion of subjects with HIV-1 RNA < 50 copies/mL by M = E and M=F approach
- The change from baseline in CD4+ Cell Count and CD4 percentage (%) by visit

The analyses for the efficacy endpoints above will be conducted based on the All B/F/TAF Analysis Set.

6.3.2. Analysis of the Efficacy Endpoints for All B/F/TAF Analysis

6.3.2.1. Analysis of the Proportion of Subjects with HIV-1 RNA < 50 copies/mL by and Missing = Excluded and Missing = Failure Approaches

The proportion of subjects with HIV-1 RNA < 50 copies/mL will be analyzed using M = E for imputing missing HIV-1 RNA values using the All B/F/TAF Analysis Set for the all B/F/TAF analysis.

- Missing = Excluded (M = E)

  In this approach, all missing data will be excluded in the computation of the percentages (ie, missing data points will be excluded from both the numerator and denominator in the computation). The denominator for percentages at a visit is the number of subjects in the all B/F/TAF analysis set with nonmissing HIV-1 RNA value at that visit.

- Missing = Failure (M = F)

  In this approach, all missing data will be treated as HIV-1 RNA ≥ 50 copies/mL. The denominator for percentages is the number of subjects in all B/F/TAF analysis set.

For M = E and M=F analyses, the number and percentage of subjects with HIV-1 RNA in the following categories will be summarized:

- < 50 copies/mL
  - < 20 copies/mL
    - < 20 copies/mL Not Detectable
    - < 20 copies/mL Detectable
  - 20 to < 50 copies/mL

- 50 to < 200 copies/mL
- 200 to < 400 copies/mL
- 400 to < 1000 copies/mL
- ≥ 1000 copies/mL
- Missing (only applicable for M=F analysis)

For all B/F/TAF analyses, the 95% CI for the proportion of subjects with HIV-1 RNA < 50 copies/mL for a treatment group will be constructed using the Clopper-Pearson exact method.

For M =F analysis, results will be summarized by visit up to Week 240 for B/F/TAF group and up to Week 96 for DTG + F/TAF to B/F/TAF group. For the M = E analysis, results will be summarized by treatment group for all visits through the end of study. No statistical comparison will be made for the all B/F/TAF analysis.

6.3.2.2. Analysis of CD4+ Cell Count and CD4%

The analysis of CD4 cell count will be based on on-treatment data (ie, up to 1 day after the last dose date of study drug) using the all B/F/TAF Analysis Set for the all B/F/TAF analysis.

The changes from baseline in CD4+ cell count at each visit will be summarized by treatment group using descriptive statistics. No statistical comparisons will be made for the all B/F/TAF analysis.

Similar analysis will be conducted for CD4% using the all B/F/TAF Analysis Set for the all B/F/TAF analysis.

In addition, the mean and 95% CI of change from baseline in CD4+ cell count over time while receiving B/F/TAF will be plotted.

6.4. Changes from Protocol-Specified Efficacy Analyses

No change from the protocol-specified efficacy analysis is planned.

7. SAFETY ANALYSES

Safety data will be summarized by treatment for the subjects in the All B/F/TAF Analysis Set for the all B/F/TAF analysis, unless specified otherwise. All safety data collected up to 30 days after permanent discontinuation of study drug B/F/TAF will be summarized by treatment group, unless specified otherwise. All safety data will be included in data listings.

For the all B/F/TAF analysis, the terms "study drug start date (ie, the first dose date)", "study drug stop date (ie, the last dose date)", and "baseline" in the text below refer to the first dose date, the last dose date, and baseline defined for the all B/F/TAF phase analysis; the term "study drug" in the text below refer to B/F/TAF.

7.1. Adverse Events and Deaths

7.1.1. Adverse Event Dictionary

Clinical and laboratory AEs will be coded using the current version of MedDRA. System organ class (SOC), high-level group term (HLGT), high-level term (HLT), preferred term (PT), and lowest-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 (mild), Grade 2 (moderate), Grade 3 (severe), or Grade 4 (life threatening) according to toxicity criteria specified in the protocol. The severity grade of events for which the investigator did not record severity will be left as "missing" for data listings.

7.1.3. Relationship of Adverse Events to Study Drug

Related AEs are those for which the investigator selected "Related" on the AE eCRF to the question of "Related to Study Treatment." 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 AEs met the definitions of SAE specified in the study protocol. Serious adverse events captured and stored in the clinical database will be reconciled with the SAEs from the Gilead Global Patient Safety (GLPS) database 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) are defined as 1 or both of the following:

- Any AEs with an onset date on or after the study drug start date and no later than 30 days after permanent discontinuation of the study drug, or
- Any AEs leading to premature discontinuation of study drug.

For the all B/F/TAF analysis, the AE onset date will be compared with the first and last dose dates for the All B/F/TAF phase analysis.

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 month and year (or year) of 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 month and year (or year) of the AE onset 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 marked as ongoing or on or after 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 Death

The number and percentage of subjects who experienced at least 1 TEAE will be provided and summarized by SOC, HLT, PT, and treatment group using All B/F/TAF Analysis Set. For other AEs described below, summaries will be provided by SOC, PT, and treatment group using the All B/F/TAF Analysis Set:

- Any Grade 2, 3, or 4 treatment-emergent AEs
- Any Grade 3 or 4 treatment-emergent AEs
- All treatment-emergent study drug-related AEs
- Any Grade 2, 3, or 4 treatment-emergent study drug-related AEs
- Any Grade 3 or 4 treatment-emergent study drug-related AEs

- All treatment-emergent SAEs
- All treatment-emergent study drug-related SAEs
- All treatment-emergent AEs that caused premature discontinuation from study drug

A brief, high-level summary of AEs described above will be provided by treatment group and by the number and percentage of subjects who experienced the above AEs. Treatment-emergent deaths observed in the study will be also included in this summary.

Treatment-emergent death refers to deaths that occurred between the first dose date and the last dose date plus 30 days (inclusive).

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 and HLT 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.

In addition to the above summary tables, all treatment-emergent AEs, Grade 3 or 4 treatment-emergent AEs, treatment-emergent study drug-related AEs, Grade 2, 3, or 4 treatment-emergent study drug-related AEs, and treatment-emergent SAEs will be summarized by PT only, in descending order of total frequency.

In addition, data listings will be provided for the following:

- All AEs
- Grade 3 and 4 AEs
- SAEs
- Study Drug-Related SAEs
- Deaths report
- AEs leading to premature discontinuation of study drug

7.1.7. Additional Analysis of Adverse Events

7.1.7.1. Stage 3 Opportunistic Illnesses in HIV

On an ongoing basis, AEs will be reviewed for events that might meet the definition of stage 3 opportunistic illnesses in HIV that are indicative of an AIDS-defining diagnoses (see Protocol Appendix 6). The Gilead medical monitor will review the possible stage 3 opportunistic illnesses and approve the events that meet the definition. Events that meet the stage 3 opportunistic illness definition of an AIDS-Defining Diagnosis will be listed.

7.1.7.2. Cardiovascular or Cerebrovascular Events

Preferred terms for defining cardiovascular or cerebrovascular events are from relevant Standardised MedDRA Query (SMQ). The selected PT listing was provided by Gilead GLPS and reviewed by Gilead medical monitors (see details in Appendix 2).

The number and percentage of subjects with treatment-emergent cardiovascular or cerebrovascular events and serious cardiovascular or cerebrovascular events by PT will be summarized for the All B/F/TAF Analysis Set. No statistical comparisons of the subject incidence rates between the 2 treatment groups will be performed. A data listing of cardiovascular or cerebrovascular events will be provided.

7.1.7.3. Hepatic Events

Preferred terms for defining hepatic events are from 15 relevant SMQs, which are identified as non-infectious and non-congenital hepatobiliary disorders. The selected PT listing was provided by Gilead GLPS and reviewed by Gilead medical monitors (see details in Appendix 3).

The number and percentage of subjects with treatment-emergent hepatic events and serious hepatic events by PT will be summarized by treatment group based on the All B/F/TAF Analysis Set. No statistical comparisons of the subject incidence rates between the 2 treatment groups will be performed. A data listing of hepatic events will be provided.

7.1.7.4. COVID-19

A data listing of AEs for COVID-19 (see definition in Appendix 4) will be provided.

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 All B/F/TAF Analysis Set only, except that the summaries (number and percentage of subjects) for treatment-emergent laboratory abnormalities will be provided for All B/F/TAF Analysis Set. 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 imputed value will be used for the purpose of calculating summary statistics as specified in Section 3.7.

A by-subject listing for laboratory test results will be provided by subject ID number and visit in chronological order for hematology, serum chemistry, and urinalysis separately for all data collected from both phases of the study. Values falling outside of the reference range and/or having a severity grade of 1 or higher on the Gilead Grading Scale for Severity of Adverse Events and Laboratory Abnormalities 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 will be provided by treatment group for each laboratory test specified in the study protocol as follows:

- Baseline values
- Values at each postbaseline analysis window
- Change from baseline at each postbaseline analysis window
- Percentage change from baseline to each postbaseline analysis window (if specified)

A baseline laboratory value will be defined as the last nonmissing value obtained on or prior to the date of first dose of study drug. Change from baseline to a postbaseline visit will be defined as the postbaseline value minus the baseline value. The mean, median, Q1, Q3, minimum, and maximum values will be displayed to the reported number of digits; SD values will be displayed to the reported number of digits plus 1.

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.8.3.

Calcium Corrected for Albumin

Calcium corrected for albumin will be calculated and summarized for the study. The following formula will be used when both serum calcium and albumin results for a given blood drawn are available and serum albumin value is < 4.0 g/dL.

- Calcium corrected for albumin (mg/dL) = serum calcium (mg/dL) + 0.8 × (4.0 – albumin (g/dL))

Toxicity grading for calcium will be applied based on the corrected values.

Estimated GFR

The following formula will be used to calculate $eGFR_{CG}$:

- $eGFR_{CG}$ (mL/min) = [(140 – age (yrs)) × weight (kg) × (0.85 if female)] / (SCr (mg/dL) × 72), where weight is total body mass in kilograms, and SCr is serum creatinine.

7.2.2. Graded Laboratory Values

The Gilead Grading Scale for Severity of Adverse Events and Laboratory Abnormalities will be used for assigning 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 (ie, increased, decreased) will be presented separately.

If there is any laboratory toxicity grading scale overlapping with the normal reference ranges (eg, grade 1 scale overlaps with normal reference ranges), laboratory values that are within the normal range will be grade 0, except for lipid tests.

For triglycerides, LDL, and cholesterol, the protocol-specified toxicity grading scale is for fasting test values, so nonfasting lipid results (or lipid results without a known fasting status) will not be graded or summarized by toxicity grades.

7.2.2.1. Treatment-Emergent Laboratory Abnormalities

Treatment-emergent laboratory abnormalities are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point, up to 30 days after permanent discontinuation of 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. Notice that the baseline toxicity grade for all B/F/TAF analysis will be based on the first dose date of B/F/TAF.

Fasting glucose and nonfasting glucose (including glucose results without a known fasting status) are graded based on different grading scales as specified in the protocol. Treatment-emergent laboratory abnormalities will be summarized for fasting glucose. Maximum postbaseline grade, instead of treatment-emergent grade, for nonfasting glucose (including glucose results without a known fasting status) will be summarized, as nonfasting glucose was not assessed at baseline visit for most of the subjects; therefore, an abnormality is treatment-emergent or not cannot be determined for these subjects.

7.2.2.2. Summaries of Laboratory Abnormalities

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

- Treatment-emergent laboratory abnormalities
- Treatment-emergent Grade 3 and 4 laboratory abnormalities
- Treatment-emergent Grade 2, 3 and 4 laboratory abnormalities

For all summaries of laboratory abnormalities, the denominator is the number of subjects with any nonmissing postbaseline values up to 30 days after last dosing date.

A by-subject listing of all treatment-emergent laboratory abnormalities and treatment-emergent Grade 3 or 4 laboratory abnormalities will be provided by subject ID number and visit in chronological order.

7.2.3. Metabolic Laboratory Evaluations

For metabolic assessments, including fasting glucose and the lipid panel (ie, total cholesterol, triglycerides, LDL, HDL, total cholesterol to HDL ratio), only those measurements under fasting status will be summarized.

In addition, the number and percentage of subjects who took lipid-modifying medication at the first dose of B/F/TAF and subjects who initiated the lipid modifying medication while receiving B/F/TAF will be provided.

A lipid-modifying medication is defined as a medication with ATC2 term = "LIPID MODIFYING AGENTS" and CMDECOD containing the wording of "STATIN".

Median (Q1, Q3) of change from baseline in fasting metabolic assessments over time will be plotted by treatment group.

7.2.4. Liver-Related Laboratory Evaluations

Liver-related abnormalities after initial study drug dosing will be examined and summarized using the number and percentage of subjects who were reported to have the following laboratory test values for postbaseline measurements:

- Aspartate aminotransferase (AST): (a) > 3 × ULN, (b) > 5 × ULN, (c) > 10 × ULN, (d) > 20 × ULN
- Alanine aminotransferase (ALT): (a) > 3 × ULN, (b) > 5 × ULN, (c) > 10 × ULN, (d) > 20 × ULN
- AST or ALT: (a) > 3 × ULN, (b) > 5 × ULN, (c) > 10 × ULN, (d) > 20 × ULN
- Total bilirubin: (a) > 1 × ULN, (b) > 2 × ULN
- Alkaline phosphatase (ALP) > 1.5 × ULN
- AST or ALT > 3 × ULN and total bilirubin: (a) > 1.5 × ULN, (b) > 2 × ULN
- AST or ALT > 3 × ULN and total bilirubin > 2 × ULN and ALP < 2 × ULN

The summary will include data from all postbaseline visits up to 30 days after the last dose of study drug. For individual laboratory tests, subjects will be counted once based on the most severe postbaseline value. For both the composite endpoint of AST or ALT and total bilirubin, and the composite endpoint of AST or ALT, total bilirubin, and ALP, subjects will be counted once when the criteria are met at the same postbaseline visit date. The denominator is the number -of subjects in the All B/F/TAF Analysis Set with nonmissing postbaseline value of the tests in evaluation at the same postbaseline visit date. Subjects with AST or ALT > 3 × ULN will also be listed.

In addition, baseline, post-baseline, and change from baseline in AST, ALT, ALP, and total bilirubin will be summarized by treatment group and visit using descriptive statistics.

Listings of liver-related laboratory tests will be provided for subjects with any AST or ALT > 3 x ULN, TB > 1 x ULN, or ALP > 1.5 x ULN while receiving B/F/TAF or subjects with treatment-emergent Grade 3 or 4 ALT, AST, ALP, and TB for all B/F/TAF analysis set.

7.2.5. Renal-Related Laboratory Evaluations

7.2.5.1. Serum Creatinine and $eGFR_{CG}$

Baseline, postbaseline, and change from baseline in serum creatinine and $eGFR_{CG}$ will be summarized by treatment group and visit using descriptive statistics.

Median (Q1, Q3) of change from baseline in serum creatinine and $eGFR_{CG}$ over time will be plotted by treatment group.

7.3. Body Weight, Height, and Vital Signs

Descriptive statistics will be provided by treatment group for vital signs and body weight as follows using the All B/F/TAF Analysis Set:

- Baseline values
- Values at each postbaseline analysis window
- Change from baseline to each postbaseline analysis window

A baseline value will be defined as the last nonmissing value obtained on or prior to the date of first dose of study drug. Change from baseline to a postbaseline visit will be defined as the postbaseline value minus the baseline value.

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.8.3. No formal statistical testing is planned.

A by-subject listing of vital signs will be provided by subject ID number and visit in chronological order. In the same listing, a by-subject listing of body weight, height, and BMI will be provided.

7.4. Prior and Concomitant Medications

7.4.1. Nonstudy Drug Antiretroviral Medications

Any nonstudy drug ARV medications used prior to, during, or after the study (if collected) will be coded using the Gilead-modified World Health Organization (WHO) Drug Dictionary for ARV medications. The WHO preferred drug name and drug code will be attached to the clinical database. All nonstudy drug ARV medications will be listed. No inferential statistics will be provided.

7.4.2. Concomitant Non-ARV Medications

Concomitant non-ARV medications (ie, medications other than study drug that are taken while receiving study drug) will be coded using the WHO Drug Dictionary. The WHO preferred drug name and drug code will be attached to the clinical database. Use of concomitant medications from Study Day 1 for All B/F/TAF analysis up to the date of last dose of study drug will be summarized (number and percentage of subjects) by treatment group, and preferred drug name. Multiple drug use (by preferred drug name) will be counted only once per subject. The summary will be sorted by decreasing total frequency of preferred drug name. For drug with the same frequency, sorting will be done alphabetically.

If the start or stop date of non-ARV medications is incomplete, the month and year (or year alone, if month is not recorded) of the start or stop date will be used to determine whether the non-ARVs are concomitant or not. The medication is concomitant if the month and year of the start or stop (or year of the start or stop, if month is not recorded) of the medication does not meet either of the following criteria:

- The month and year of start of the medication is after the date of the last dose of study drug
- The month and year of stop of the medication is before the date of the first dose of study drug

If the start and stop date of non-ARV medications are complete, the start date is not after last dose date and the stop date is not before first dose date, or the non-ARV medications are marked as ongoing and start date is on or before last dose date, the non-ARV medications are concomitant.

Summaries of non-ARV concomitant medications will be provided for the All B/F/TAF Analysis Set. Subjects with any concomitant non-ARV medications will be listed. No inferential statistics will be provided.

7.5. Electrocardiogram Results

A shift table for all B/F/TAF analysis of the investigators' assessment of ECG results at each scheduled postbaseline visit compared with baseline values will be presented by treatment group using the following categories: normal; abnormal, not clinically significant; abnormal, clinically significant; or missing. The number and percentage of subjects in each cross-classification group of the shift table will be presented. Subjects with a missing value at baseline or postbaseline will not be included in the denominator for percentage calculation. Summary of ECG results will be presented by treatment groups for the All B/F/TAF Analysis Set. No inferential statistics will be provided.

A by-subject listing for ECG assessment results will be provided by subject ID number and visits in chronological order.

7.6. Other Safety Measures

A data listing will be provided for subjects experiencing pregnancy during the study. Physical examination data was not collected in the eCRF. Therefore, it will not be included in the analysis.

7.7. Changes from Protocol-Specified Safety Analyses

No change from the protocol-specified safety analysis is planned.

8. PHARMACOKINETIC ANALYSES

All necessary summaries on pharmacokinetic analyses have been performed as part of Week 48 CSR, and will not be repeated in the final analysis.

9. SPECIAL POPULATION ANALYSES

Special population analyses will be performed using for the All B/F/TAF Analysis Set only.

9.1. Analyses for HIV/HBV Coinfected Subjects

For all B/F/TAF analyses, subjects with HIV/HBV coinfection at baseline (ie. at the first dose of B/F/TAF) are defined as subjects who meet any of the following two criteria:

- Positive HBsAg on or prior to the first dose date of B/F/TAF (including both phases), or
- Negative HBsAg, negative HBsAb, positive HBcAb, and quantifiable HBV DNA (ie, HBV DNA ≥ 20 IU/mL) on or prior to the first dose date of B/F/TAF (including both phases).

The following listings will be provided for subjects with HIV/HBV coinfection at baseline:

- Listing of adverse events
- Listing of liver-related laboratory tests and HBV DNA results

Subjects with incident HIV/HBV coinfection while on study drug (if any) are defined as subjects who are not HIV/HBV coinfected at baseline for all B/F/TAF analyses and meet any of the following criteria:

- Positive HBsAg after the first dose date of B/F/TAF (including both phases) and on or prior to the date of permanent discontinuation of B/F/TAF (including both phases), or
- Negative HBsAg, negative HBsAb, positive HBcAb, and quantifiable HBV DNA (ie, HBV DNA ≥ 20 IU/mL) after the first dose date of B/F/TAF (including both phases) and on or prior to the date of permanent discontinuation of B/F/TAF (including both phases), or
- Experience any of the following adverse events (ie, selected MedDRA PTs from the SMQ of "Liver Infections") after the first dose date of B/F/TAF (including both phases) and on or prior to the date of permanent discontinuation of B/F/TAF (including both phases): Acute hepatitis B, Chronic hepatitis B, Congenital hepatitis B infection, Hepatitis B, Hepatitis B core antibody positive, Hepatitis B DNA assay positive, Hepatitis B surface antigen positive, Hepatitis B virus test positive.

The following listings will be provided for subjects with incident HIV/HBV coinfection while on B/F/TAF (if any):

- Listing of adverse events
- Listing of liver-related laboratory tests and HBV DNA results

9.2. Analyses for HIV/HCV Coinfected Subjects

For all B/F/TAF analysis, subjects with HIV/HCV coinfection at baseline (ie, at the first dose of B/F/TAF) are defined as subjects with positive HCVAb and quantifiable HCV RNA (ie, HCV RNA ≥ 15 IU/mL) on or prior to the first dose date of B/F/TAF (including both phases). The following analyses will be provided for subjects with HIV/HCV coinfection at baseline:

- Listing of adverse events
- Listing of liver-related laboratory tests and HCV RNA results

Subjects with incident HIV/HCV coinfection while on study drug for all B/F/TAF analysis are defined as subjects who are not HIV/HCV coinfected at baseline for all B/F/TAF analysis and meet any of the following criteria:

- Positive HCVAb after the first dose date of B/F/TAF (including both phases) and on or prior to the date of permanent discontinuation of B/F/TAF (including both phases) with baseline HCVAb Negative or missing, or
- Quantifiable HCV RNA (ie, HCV RNA ≥ 15 IU/mL) after the first dose date of B/F/TAF (including both phases) and on or prior to the date of permanent discontinuation of B/F/TAF (including both phases), or
- Experience any of the following adverse events (ie, selected MedDRA PTs from the SMQ of "Liver Infections") after the first dose date of B/F/TAF (including both phases) and on or prior to the date of permanent discontinuation of B/F/TAF (including both phases): Acute hepatitis C, Chronic hepatitis C, Hepatitis C, Hepatitis C antibody positive, Hepatitis C RNA positive, Hepatitis C virus test positive.

The following listings will be provided for subjects with incident HIV/HCV coinfection while on B/F/TAF:

- Listing of adverse events
- Listing of liver-related laboratory tests and HCV RNA results

10. REFERENCES

U. S. Department of Health and Human Services, Food and Drug Administration (FDA), Center for Drug Evaluation and Research (CDER). Human Immunodeficiency Virus-1 Infection: Developing Antiretroviral Drugs for Treatment. Guidance for Industry. Silver Spring, MD. November, 2015.

11. SOFTWARE

SAS® Version 9.4 (SAS Institute Inc., Cary, NC.) is to be used for all programming of tables, listings, and figures.

nQuery Advisor® Version 6.0 (Statistical Solutions, Cork, Ireland.) is to be used for sample size and power calculation.

12. SAP REVISION

Revision Date (dd month, yyyy)	Section	Summary of Revision	Reason for Revision

13. APPENDICES

Appendix 1. Study Procedures Table
Appendix 2. Cardiovascular or Cerebrovascular Events
Appendix 3. Hepatic Events
Appendix 4. Adverse Events of COVID-19
Appendix 5. Determining Missing and Virtual Visits Due to COVID-19
Appendix 6. Programming Specification

Appendix 1. Study Procedures Table

Appendix Table 1. Study Procedures Table (Blinded Phase)

Study Procedures	Screening[a]	Day 1[b]	End of Week[e, q]														Post-Week 144[e, r]	End of Blinded Treatment Visit	30-Day Follow-up[p]	Early Study Drugs DC[c]
			4	8	12	24	36	48	60	72	84	96	108	120	132	144	Every 12 Weeks			
Informed Consent	X																			
Medical History	X																			
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[f]	X[f]
Complete/Symptom- Directed Physical Exam	X	X	X[d]	X[d]	X[d]	X	X[d]	X	X[d]	X[d]	X[d]	X	X[d]	X[d]	X[d]	X	X[d]	X	X[d,f]	X[f]
12-Lead ECG (performed supine)	X	X				X		X				X				X	X[w]	X		X
Questionnaires		X	X		X			X												
Height	X																			
Vital signs (blood pressure, pulse, respiration rate, and temperature), including Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urinalysis	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[f]	X[f]
Urine Pregnancy Test[g]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Serum Pregnancy Test	X																			
Chemistry Profile[h]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[f]	X[f]
Metabolic Assessments[i]		X			X	X		X		X		X		X		X	X	X		
Estimated Glomerular Filtration Rate	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[f]	X
Hematology Profile[j]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[f]	X[f]
Plasma HIV-1 RNA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
CD4+ Cell Count	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
CCI																				

Study Procedures	Screening[a]	Day 1[b]	End of Week[e, q] 4	8	12	24	36	48	60	72	84	96	108	120	132	144	Post-Week 144[e, r] Every 12 Weeks	End of Blinded Treatment Visit	30-Day Follow-up[p]	Early Study Drugs DC[c]
HCV Serology[u]	X							X				X				X	X			
HIV-1 Genotype[k]	X																			
HIV-1 Genotype/Phenotype[e]																				X[e]
Single PK Sample[l]				X		X	X													
Trough and Post Dose PK Sample[m]			X		X															
CCI																				
Randomization[v]		X																		
Provide subject dosing diary to subjects		X	X	X	X	X														
CCI																				
CCI																				
HBV blood panel[t]	X				X[t]	X[t]		X[t]		X[t]		X[t]		X[t]		X[t]	X			
Plasma HBV DNA[t]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X
Study Drug Dispensation		X[b]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[s]		
Study Drug Accountability			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X

a Evaluations to be completed within 30 days prior to Day 1.
b Initiation of the first dose of study drug is to take place in-clinic following completion of study procedures at the Day 1 visit.
c Early Study Drugs Discontinuation visit to occur within 72 hours of last dose of study drug. Subjects will be asked to continue attending the scheduled study visits through the End of Blinded Treatment Visit even if the subject discontinues study drug.
d Symptom-directed physical examination as needed.
e HIV-1 genotype and phenotype testing for subjects with virologic failure. Following virologic rebound, subjects will be asked to return to the clinic (2-3 weeks later) prior to the next scheduled visit or at the next scheduled study visit, for a HIV-1 RNA and HIV-1 genotype and phenotype (reverse transcriptase, protease and integrase genotype and phenotype) blood draw. Based on the results of this testing, subjects should be managed according to the Virologic Rebound Schema (Protocol Section 6.12).
f Any adverse event or test showing abnormal results that is believed to have a possible or probable causal relationship with the study drug will be repeated weekly (or as often as deemed prudent by the Investigator) until the abnormality is resolved, returns to baseline, or is otherwise explained.
g Females of childbearing potential only. Positive urine pregnancy tests will be confirmed with a serum test.

h Chemistry profile: alkaline phosphatase, AST, ALT, GGT, total bilirubin, direct and indirect bilirubin, total protein, albumin, LDH, CPK, bicarbonate, BUN, calcium, chloride, creatinine, glucose, phosphorus, magnesium, potassium, sodium, uric acid and amylase (reflex lipase testing is performed in subjects with total amylase > 1.5 x ULN). At Day 1, Weeks 12, 24, 48, 72, 96, 120 and 144, every 24 weeks post Week 144, and End of Blinded Treatment Visit, analyses of glucose will be done as part of the fasting metabolic assessments every 24 weeks and not as part of the chemistry profile. Additionally: TSH will be analyzed at Screening, Day 1, Weeks 24, 48, 72, 96, 120, and 144 followed by every 24 weeks post Week 144, End of Blinded Treatment Visit and Early Study Drugs Discontinuation visit. PT/INR to be performed at Day 1.

i Fasting (no food or drinks, except water, at least 8 hours prior to blood collection) glucose and lipid panel (total cholesterol, HDL, direct LDL, triglycerides). If the subject has not fasted prior to the visit, the visit may proceed, but the subject must return within 72 hours in a fasted state to draw blood for the metabolic assessments.

j CBC with differential and platelet count.

k The Investigator must have received the results from the screening genotype report before proceeding with the Day 1 visit. Screening genotype report must show sensitivity to TFV and FTC. If genotype results from a local laboratory obtained ≤ 90 days prior to screening visit date show sensitivity to these drugs, this genotype will be acceptable to fulfill this inclusion criterion in the event that the genotype obtained at screening is not yet available and all other inclusion/exclusion criteria have been confirmed.

l A single PK blood sample will be collected at any time pre or post-dose

m A trough PK blood sample will be collected between 20-28 hours following the last dose. Following an observed dose, a single post dose blood sample will be collected between 1 and 4 hours post dose.

[redacted]

[redacted]

p Only required for those subjects not enrolling in the open-label rollover extension, those subjects who prematurely discontinue study drugs and do not continue in the study through at least one subsequent visit after the Early Study Drugs Discontinuation Visit. For the purpose of scheduling a 30-Day Follow-Up Visit, a ± 6 days window may be used.

q Study visits are to be completed within ± 2 days of the protocol-specified visit date based on the Day 1 visit through Week 12 and completed within ± 6 days through to Week 144, unless otherwise specified. The visit window at Weeks 48, 96, and 144 will be ± 6 weeks of the protocol-specified visit date.

r After Week 144, all subjects will continue to take their blinded study drug and attend visits every 12 weeks until the End of Blinded Treatment Visit. Visit window of ± 6 days for study visits post Week 144.

s Open-label study drug, B/F/TAF FDC will be dispensed to subjects participating in the Open-Label Rollover extension for up to 48 weeks.

t HBV blood panel will be performed at Screening (Hepatitis B virus surface antigen (HBsAg), Hepatitis B virus surface antibody (HBsAb) and Hepatitis B virus core antibody (HBcAb)). For subjects who meet the definition of HBV infection at any visit: The following will be conducted by the central laboratory: HBsAb, HBsAg (qualitative and quantitative) and HBeAg (if negative, reflex HBeAb) (Weeks 12, 24, 48, 72, 96 and every 24 weeks post Week 96) and Plasma HBV DNA (every visit). For subjects who do NOT meet the definition of HBV infection at any visit: The following will be conducted by the central laboratory: Hepatitis B surface antibody (HBsAb), Hepatitis B virus core antibody (HBcAb), and Hepatitis B virus surface antigen serology (HBsAg). Subjects who are HBsAg and/or HBcAb positive will have a reflex test for HBV DNA (viral load) (Week 48, 96 and 144 and every 48 weeks post Week 144)

u Hepatitis C virus (HCVAb) serology. Subjects who are HCVAb positive will have a HCV RNA test performed (Week 48, 96 and 144 and every 48 weeks post Week 144)

v Randomization may be performed up to 3 days prior to the in-clinic Day 1 visit provided that all screening procedures have been completed and subject eligibility has been confirmed.

w To be performed every 48 weeks.

Appendix Table 2. Study Procedures Table (Open-Label Rollover Extension)

Study Procedures	End of Blinded Treatment Visit[a]	End of Week[e, l, o]								30-Day Follow-up[k]	Early Study Drugs DC[c]
		12 OL	24 OL	36 OL	48 OL	60 OL	72 OL	84 OL	96 OL		
Adverse Events	X	X	X	X	X	X	X	X	X	X[f]	X[f]
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X
Complete/Symptom-Directed Physical Exam	X	X[d]	X[d]	X[d]	X	X[d]	X[d]	X[d]	X	X[d,f]	**X**[f]
12-Lead ECG (performed supine)	X				X				X		
Vital signs (blood pressure, pulse, respiration rate, and temperature), including Weight	X	X	X	X	X	X	X	X	X	X	X
Urinalysis	X	X	X	X	X	X	X	X	X	X[f]	X[f]
Urine Pregnancy Test[g]	X	X	X	X	X	X	X	X	X	X	X
Chemistry Profile[h]	X	X	X	X	X	X	X	X	X	X[f]	X[f]
Metabolic Assessments[i]	X		X		X		X		X		
Estimated Glomerular Filtration Rate	X	X	X	X	X	X	X	X	X	X[f]	X
Hematology Profile[j]	X	X	X	X	X	X	X	X	X	X[f]	X[f]
Plasma HIV-1 RNA	X	X	X	X	X	X	X	X	X	X	X
CD4+ Cell Count	X	X	X	X	X	X	X	X	X	X	X
CCI											
HBV Blood Panel[m]			X[m]		X[m]		X[m]		X[m]		
Plasma HBV DNA[m]		X[m]	X[m]	X[m]	X[m]	X[m]	X[m]	X[m]	X[m]		
HCV Serology[n]					X[n]				X[n]		
HIV-1 Genotype/Phenotype[e]											X[e]
Study Drug Dispensation[b]	X[b]	X	X	X	X	X	X	X			
Study Drug Accountability	X	X	X	X	X	X	X	X	X		X

a Once the last subject completes the Week 144 visit and Gilead completes the Week 144 analysis, all subjects will return to the clinic (within 30 days ± 6 days) for an End of Blinded Treatment Visit. At the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF FDC is demonstrated following review of unblinded data, subjects in a country where GS-9883/F/TAF FDC is not available, will be given the option to receive B/F/TAF FDC in an open-label extension phase for up to 48 weeks, or until the product becomes accessible to subjects through an access program, or until Gilead Sciences elects to discontinue the study in that country, whichever occurs first.

b Open-label study drug, B/F/TAF FDC will be dispensed to subjects participating in the Open-Label Rollover extension for up to 48 weeks.
c Subjects who discontinue study drug during the open-label rollover extension portion of the study will be asked to return to the clinic within 72 hours of stopping study drugs for the Early Study Drugs Discontinuation Visit followed by a 30-Day Follow-Up Visit. The subject will not continue attending the scheduled study visits.
d Symptom-directed physical examination as needed.
e HIV-1 genotype and phenotype testing for subjects with virologic failure. Following virologic rebound, subjects will be asked to return to the clinic (2-3 weeks later) prior to the next scheduled visit or at the next scheduled study visit, for a HIV-1 RNA and HIV-1 genotype and phenotype (reverse transcriptase, protease, and integrase genotype and phenotype) blood draw. Based on the results of this testing, subjects should be managed according to the Virologic Rebound Schema (Protocol Section 6.12.1).
f Any adverse event or test showing abnormal results that is believed to have a possible or probable causal relationship with the study drug will be repeated weekly (or as often as deemed prudent by the Investigator) until the abnormality is resolved, returns to Day 1, or is otherwise explained.
g Females of childbearing potential only. Positive urine pregnancy tests will be confirmed with a serum test.
h Chemistry profile: alkaline phosphatase, AST, ALT, GGT, total bilirubin, direct and indirect bilirubin, total protein, albumin, LDH, CPK, bicarbonate, BUN, calcium, chloride, creatinine, glucose, phosphorus, magnesium, potassium, sodium, uric acid and amylase (reflex lipase testing is performed in subjects with total amylase > 1.5 x ULN). At Week 24 OL and Week 48 OL, and End of Blinded Treatment Visit, analyses of glucose will be done as part of the fasting metabolic assessments and not as part of the chemistry profile. For all subjects, TSH will be done at the End of Blinded Treatment Visit, Week 24 OL, Week 48 OL, and Early Study Drug Discontinuation Visit.
i Fasting (no food or drinks, except water, at least 8 hours prior to blood collection) glucose and lipid panel (total cholesterol, HDL, direct LDL, triglycerides) every 24 weeks. If the subject has not fasted prior to the visit, the visit may proceed, but the subject must return within 72 hours in a fasted state to draw blood for the metabolic assessments.
j CBC with differential and platelet count.
k Subjects who complete the open-label rollover extension will be required to return to the clinic 30 days after the completion of study drugs for the 30-Day Follow-Up Visit. Subjects who permanently discontinue study drugs during the open-label rollover extension will be asked to return to the clinic 30 days after the completion of the Early Study Drugs Discontinuation Visit for the 30-Day Follow-Up Visit. For the purpose of scheduling a 30-Day Follow-Up Visit, a ± 6 days window may be used.
l Study visits are to be completed within ± 2 days of the protocol-specified visit date based on the End of Blinded Treatment Visit date through Week 12 OL and completed within ± 6 days of the protocol-specified visit date every 12 weeks thereafter, unless otherwise specified
m For subjects who meet the definition of HBV infection at any visit: The following will be conducted by the central laboratory: HBsAb, HBsAg (qualitative and quantitative) and HBeAg (if negative, reflex HBeAb) (every 24 weeks) and Plasma HBV DNA (every 12 weeks). For subjects who do NOT meet the definition of HBV infection at any visit: The following will be conducted by the central laboratory: Hepatitis B surface antibody (HBsAb), Hepatitis B virus core antibody (HBcAb), and Hepatitis B virus surface antigen serology (HBsAg). Subjects who are HBsAg and/or HBcAb positive will have a reflex test for HBV DNA (viral load) (Weeks 48 OL and 96 OL)
n Hepatitis C virus (HCVAb) serology. Subjects who are HCVAb positive will have a HCV RNA test performed. (Weeks 48 OL and 96 OL).
o After Week 96 OL, if subject is in a country where GS-9883/F/TAF is not available, the study procedures completed by the subject will be the same at every 48 weeks (i.e. OL Weeks 48, 96) and at every 12 weeks (i.e. OL Weeks 12, 24. 36, 60, 72, 84) until the product becomes accessible to subjects through an access program, or until Gilead Sciences elects to discontinue the study in that country, whichever occurs first.

Appendix 2. Cardiovascular or Cerebrovascular Events

An adverse event record will be flagged as a cardiovascular or cerebrovascular event if its MedDRA PT is included in the pre-specified PT list, which includes all PTs from the narrow search of the following 3 SMQs under MedDRA version 24.0 provided by Gilead GLPS and reviewed by Gilead medical monitors.

	SMQ Source
Cardiovascular or Cerebrovascular Events	Ischaemic central nervous system vascular conditions (SMQ) – Narrow Scope Term
	Myocardial infarction (SMQ) - Narrow Scope Term
	Other ischaemic heart disease (SMQ) - Narrow Scope Term

Appendix 3. Hepatic Events

An adverse event record will be flagged as a hepatic event if its MedDRA PT is included in the pre-specified PT list, which includes all PTs from the broad search of the following 15 SMQs under MedDRA version 24.0 provided by Gilead GLPS and reviewed by Gilead medical monitors.

	SMQ Source
Hepatic Events (HEP)	Biliary neoplasms benign (incl cysts and polyps) (SMQ)
	Biliary malignant tumours (SMQ)
	Biliary tumours of unspecified malignancy (SMQ)
	Biliary system related investigations, signs and symptoms (SMQ)
	Biliary tract disorders (SMQ)
	Gallbladder related disorders (SMQ)
	Gallstone related disorders (SMQ)
	Cholestasis and jaundice of hepatic origin (SMQ)
	Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions (SMQ)
	Hepatitis, non-infectious (SMQ)
	Liver neoplasms, benign (incl cysts and polyps) (SMQ)
	Liver malignant tumours (SMQ)
	Liver tumours of unspecified malignancy (SMQ)
	Liver related investigations, signs and symptoms (SMQ)
	Liver-related coagulation and bleeding disturbances (SMQ)

Appendix 4. Adverse Events of COVID-19

An adverse event record will be flagged as adverse events for COVID-19 if its MedDRA PT is included in the pre-specified PT list, which includes all PTs from the narrow search of the following COVID-19 SMQs under MedDRA version 24.0 provided by Gilead GLPS (search name: COVID-19 (SMQ) – Narrow) and reviewed by Gilead medical monitors.

	SMQ Source
AEs for COVID-19	**COVID-19 (SMQ) (Narrow Scope)**

Appendix 5. Determining Missing and Virtual Visits Due to COVID-19

This appendix describes the site collection of COVID-19 data as pertains to missed/virtual visits and the data processing algorithm used to determine which visits were missing and which visits were virtual.

Data collection

A COVID-19 supplement to the eCRF Completion Guidelines (CCG) was provided by data management to instruct clinical trial sites with respect to data entry expectations pertaining to scenarios related to the COVID-19 pandemic. If a visit was missed, sites should enter "Visit missed due to COVID-19." If a visit which was to be conducted in-person was conducted virtually, sites should enter "Virtual visit due to COVID-19."

Determination of Missed and Virtual visits

Natural Language Processing (NLP) was used to search the CRF comment fields to identify instances of "COVID-19" (or synonyms, see Table X 1) and "Virtual" (or synonyms, see Table X 1). The search terms are maintained in a global lookup and can be modified and/or corrected to tune the NLP model. For each comment field the following algorithm was applied:

STEP 1: Eliminate extraneous text from each comment field, e.g. "and", "or", "for", etc. This is done using the list of extraneous terms given in Table X 2.

STEP 2: Check each of the remaining comment text strings against the "COVID-19" terms and "Virtual" terms with the Levenshtein distance, using SAS function COMPGED (Computes a generalized edit distance using the Levenshtein operations to compute/summarize the degree of difference between two text strings):

i. If Levenshtein distance < 149 for any of the "COVID-19" terms then COVIDFL = 1, else COVIDFL = 0

ii. If Levenshtein distance < 149 for any of the "Virtual" terms then VIRTFL = 1, else VIRTFL = 0

STEP 3: For any comments with COVIDFL = 1, assign "Missed visit" or "Virtual visit as follows

i. IF COVIDFL =1 and the visit date is missing then result is 'Missed Visit'

ii. IF COVIDFL =1 and VIRTFL = 1 then result is = 'Virtual Visit'

iii. Otherwise result is missing

Table X 1. Examples of search terms for "COVID-19" and "Virtual" used to identify missed and virtual visits

Search terms for "COVID-19"	Search terms for "Virtual"
COVID19	VIRTUAL
CORONA	TELEMED
CORONAVIRUS	TELEHEALTH
PANDEMIC	TELEPHONE
OUTBREAK	REMOTE
CRISIS	TELEMEDICINE
LOCKDOWN	TELECONSULTATION
QUARANTINE	TELEPHONICALLY
SHELTER	PHONE
	HOME VISIT
	ZOOM
	SKYPE

Table X 2. Examples of extraneous text terms to eliminate from the comment fields.

a	down	in	she'd	until
about	during	into	she'll	up
above	each	is	she's	very
after	few	it	should	was
again	for	its	so	we
against	from	it's	some	we'd
all	further	itself	such	we'll
am	had	i've	than	were
an	has	let's	that	we're
and	have	me	that's	we've
any	having	more	the	what
are	he	most	their	what's
as	he'd	my	theirs	when
at	he'll	myself	them	when's
be	her	nor	themselves	where
because	here	of	then	where's
been	here's	on	there	which
before	hers	once	there's	while
being	herself	only	these	who
below	he's	or	they	whom
between	him	other	they'd	who's
both	himself	ought	they'll	why
but	his	our	they're	why's
by	how	ours	they've	with
could	how's	ourselves	this	would
did	i	out	those	you
do	i'd	over	through	you'd
does	if	own	to	you'll
doing	i'll	same	too	your
down	i'm	she	under	you're
	you've	yourself	yourselves	yours

Appendix 6. Programming Specification

1) AGE calculated as follows: two age variables will be derived, one is for randomized phase analysis, and one is for all B/F/TAF analysis

   (i) AGE (years) for randomized phase analysis is calculated from the number of days between the date of birth (DOB) and Day 1 (Study Day 1 for the randomized phase analysis);

   (ii) AGE (years) for all B/F/TAF analysis is calculated from the number of days between the date of birth (DOB) and Day 1 (Study Day 1 for the all B/F/TAF analysis).

      a) Use the SAS INTCK function to determine the number of "1st-of-month days" (eg, January 1st, February 1st, March 1st) between DOB and Day 1 (inclusive),

      b) Divide the result in (b) by 12,

      c) AGE = the integer of the result in (c),

      d) If the DOB and Day 1 have the month in common and the birthday is later in the month than the date of Study Day 1, then subtract one from the AGE result above.

   For subjects randomized and never dosed with study drug, age will be calculated from the date of randomization.

2) All screened subjects refer to all subjects who are screened (ie, with nonmissing screening date) and have a screening number. For summaries, the same subject is counted only once. DOB and other demographic information such as sex, race, ethnicity, country, and initials will be used to identify unique screened subjects.

3) Screen failure subjects are the subjects who are screened and answered "No" for any inclusion criteria or "Yes" for any exclusion criteria regardless of which version of protocol the subject was consent to.

4) Subjects in the randomized Analysis Set are defined as subjects randomized into the study. IXRSRAND is the source to determine whether the subject is randomized (ie, subject with nonmissing RGMNDTN in the IXRSRAND dataset) and confirmed by the eCRF ENROLL dataset (ie, ENROLLYN = "Yes" in ENROLL dataset).

5) The Safety Analysis Set will include all subjects who (1) are randomized into the randomized phase of the study and (2) have received at least 1 dose of the randomized study drug. Subjects will be grouped according to the treatment they actually received.

6) The Full Analysis Set (FAS) will include all subjects who (1) are randomized into the randomized phase of the study and (2) have received at least 1 dose of the randomized study drug. Subjects will be grouped according to the treatment to which they were randomized

7) Randomized treatment (ie, TRT01P in ADSL) are derived from IXRSRAND, while actual treatment received (ie, TRT01A in ADSL) is assigned as the randomized treatment if subject took at least 1 dose of study drug and assigned as blank if subject never dosed.

8) Enrollment by Stratum: using actual HIV-1 RNA or CD4+ cell count screening value, the last screening value (with visitnum < 0) prior to randomization date and time.

9) In disposition table, the reasons for premature discontinuation are displayed in the order as they appear on the eCRF.

10) Body mass index (BMI) and Body Surface Area (BSA)

    BMI and BSA will be calculated only at baseline as follows:

    - BMI = (weight [kg]) / (height [meters]^2)
    - BSA (m^2) = SQRT([Height(cm) × Weight(kg)] / 3600)

    Baseline height and weight will be used for this calculation.

11) Please note, "Not Permitted", "Unknown", or missing categories will be excluded for percentage calculation and also excluded for p value generation for categorical data analysis (eg, CMH test or Fisher exact test). Except for Mode of infection (HIV Risk Factors), where "Unknown" will be included for percentage calculation, since a subject may fit more than 1 HIV risk factors, therefore percentage may add to more than 100% and no p-value will be generated.

    Subjects with Race = "Not Permitted" will also be excluded to define Race subgroup (ie, black vs. nonblack) for efficacy subgroup analysis.

12) Last Dose Date and Last Study Date

    a) Last Dose Date (ie, TR01EDT or TR01EDTC for randomized phase last dose date, and TR02EDT or TR02EDTC for extension phase last dose date) in ADSL.

       Randomized Phase Last Dose Date:

       For **B/F/TAF** or **DTG/F/TAF** subjects with a partial last dosing date (ie, month and year of last dose are known), the minimum of {(extension phase first dose date – 1 day, if available), (the latest of the dispensing dates of study drug bottles, study drug start dates and end dates (based on EX dataset with study drug in randomized phase), and the imputed last dose date [day imputed as 15])} will be used as the final imputed last dose date. However, if dispensing date's month is after last dose date's month, data query is needed. If subject died and the death date is complete (ie, not partial date) and before the imputed last dose date, the complete death date should be used as the imputed last dose date.

Extension Phase Last Dose Date:

For subjects with a partial last dosing date (ie, month and year of last dose are known), the minimum of { (the latest of the dispensing dates of study drug bottles, study drug start dates and end dates (based on EX dataset with study drug in extension phase), and the imputed last dose date [day imputed as 15])} will be used as the final imputed last dose date. However, if dispensing date's month is after last dose date's month, data query is needed. If subject died and the death date is complete (ie, not partial date) and before the imputed last study date, the complete death date should be used as the imputed last study date.

b) Last Study Date is the latest of the randomized or extension phase (if available) study drug start dates and end dates, the clinic visit dates, and the laboratory visit dates, including the 30-day follow-up visit date. If study drug start dates or end dates is partially missing (ie, only year and month are known), the day will be imputed as 15 for the purpose of this analysis.

If subject died and the death date is complete (ie, not partial dat104381e) and before the imputed last study date, the complete death date should be used as the imputed last study date.

13) Toxicity Grades:

Two type of treatment emergent lab abnormalities flag variables will be derived for laboratory data as applicable. For treatment emergent flag used in listing for randomized analysis set, the baseline toxicity grade will be based on baseline value defined as the last nonmissing value obtained on or prior to the first dose of randomized study drug. For treatment emergent flag used for the All B/F/TAF analysis summary and listing using all B/F/TAF analysis set, the baseline toxicity grade will be based on baseline value defined as the last nonmissing value obtained on or prior to the first dose of B/F/TAF.

Treatment-emergent laboratory abnormalities will be summarized for all B/F/TAF analysis, following the same rules bellow.

a) For toxicity grade summaries, include all post-baseline graded results up to 30 days after the last dose of study drug B/F/TAF, not just those used in by-visit summaries.

b) For glucose grading, as specified in SAP Section 7.2.2.1, the treatment-emergent flag cannot be determined for nonfasting glucose (including glucose results without a known fasting status). As a result, these records will be excluded from the "Maximum Treatment-emergent Toxicity Grade" summary in the "Treatment-emergent Laboratory Abnormalities" or "Treatment-emergent Grade 3 or 4 Laboratory Abnormalities" summary tables. In addition, fasting glucose and non-fasting glucose will be listed as two separate laboratory tests in the "Laboratory Abnormalities" and "Grade 3 or 4 Laboratory Abnormalities" listings. Only a maximum postbaseline toxicity flag will be displayed and the treatment-emergent flag will not be displayed for nonfasting glucose as the treatment-emergent flag cannot be determined for nonfasting glucose.

14) TEAE

Events with Missing Onset Day and/or Month

An AE is treatment emergent if the following 3 criteria are met:

(1) The month and year (or year) of onset date is the same as or after the month and year (or year) of the first dose of study drug, and

(2) The month and year (or year) of the onset date is the same as or before the month and year (or year) of the 30th day after the date of the last dose of study drug, and

(3) End date is as follows:

a) The (complete) end date is on or after the first dose date, or

b) The month and year (or year) of end date is the same or after the month and year (or year) of the first dose of study drug, or

c) End date is completely missing

Events with Completely Missing Onset Date

An AE with a completely missing onset date is defined as TEAE if end date meets any of the criteria specified in 3) above.

15) Graded Laboratory Abnormalities Summary

The following labels will be used for treatment-emergent laboratory abnormalities and treatment-emergent Grade 3 or 4 laboratory abnormalities summary tables and listings:

Battery	Lab Test Label Used in l-labtox Listing	Toxicity Direction	Lab Test Label Used in t-labtox Table
Hematology	Hemoglobin	Decrease	Hemoglobin (Decreased)
	Neutrophils	Decrease	Neutrophils (Decreased)
	Platelets	Decrease	Platelets (Decreased)
	WBC	Decrease	WBC (Decreased)
Chemistry	Albumin	Decrease	Albumin (Decreased)
	Alkaline Phosphatase	Increase	Alkaline Phosphatase (Increased)
	ALT	Increase	ALT (Increased)
	Amylase	Increase	Amylase (Increased)
	AST	Increase	AST (Increased)
	Bicarbonate	Decrease	Bicarbonate (Decreased)

Battery	Lab Test Label Used in l-labtox Listing	Toxicity Direction	Lab Test Label Used in t-labtox Table
	Corrected Calcium	Increase	Corrected Calcium (Hypercalcemia)
	Corrected Calcium	Decrease	Corrected Calcium (Hypocalcemia)
	Creatine Kinase (CK)	Increase	Creatine Kinase (Increased)
	Creatinine	Increase	Creatinine (Increased)
	GGT	Increase	GGT (Increased)
	Lipase	Increase	Lipase (Increased)
	Magnesium	Decrease	Magnesium (Hypomagnesemia)
	Phosphate	Decrease	Phosphate (Hypophosphatemia)
	Serum Glucose (Fasting)	Increase	Serum Glucose (Fasting, Hyperglycemia)
	Serum Glucose (Fasting)	Decrease	Serum Glucose (Fasting, Hypoglycemia)
	Serum Glucose (Nonfasting)	Increase	Serum Glucose (Nonfasting, Hyperglycemia)
	Serum Glucose (Nonfasting)	Decrease	Serum Glucose (Nonfasting, Hypoglycemia)
	Serum Potassium	Increase	Serum Potassium (Hyperkalemia)
	Serum Potassium	Decrease	Serum Potassium (Hypokalemia)
	Serum Sodium	Increase	Serum Sodium (Hypernatremia)
	Serum Sodium	Decrease	Serum Sodium (Hyponatremia)
	Total Bilirubin	Increase	Total Bilirubin (Hyperbilirubinemia)
	Total Cholesterol (Fasting)	Increase	Total Cholesterol (Fasting, Hypercholesterolemia)
	Triglycerides (Fasting)	Increase	Triglycerides (Fasting, Increased)
	LDL (Fasting)	Increase	LDL (Fasting, Increased)
	Urea Nitrogen (BUN)	Increase	Urea Nitrogen (Increased)
	Uric Acid	Increase	Uric Acid (Hyperuricemia)
	Uric Acid	Decrease	Uric Acid (Hypouricemia)
Urinalysis	Urine Blood (Dipstick)	Increase	Urine RBC (Hematuria, Quantitative or Dipstick)*
	Urine Glucose	Increase	Urine Glucose (Glycosuria)
	Urine Protein	Increase	Urine Protein (Proteinuria)
	Urine RBC (Quantitative)	Increase	Urine RBC (Hematuria, Quantitative or Dipstick)*

* Due to the reflexive nature of the quantitative urine RBC test, results will be combined with the dipstick test of urine blood as described below. General rule is that urine RBC (Quantitative) should always be used first (if available), no matter it is collected at the same time of Urine Blood (Dipstick) or not. The combined Urine RBC (hematuria, Quantitative or Dipstick) toxicity grade will be used for "Maximum treatment-emergent toxicity grade" summary.

Is Post-BL Urine RBC (Quant.) Result Available?	Is BL Urine RBC (Quant.) Result Available?	Is Post-BL Urine Blood (Dipstick) Result Available?	Is BL Urine Blood (Dipstick) Result Available?	How to Determine Treatment-Emergent Toxicity for "Urine RBC (Hematuria, Quantitative or Dipstick)"
Yes	Yes	-	-	Compare post-BL Urine RBC (Quant.) toxicity grade to BL Urine RBC (Quant.) toxicity grade. If post-BL toxicity is greater than BL toxicity, then treatment-emergent
Yes	No	-	-	Treatment-emergent. Use post-BL Urine RBC (Quant.) toxicity grade.
No	-	Yes	Yes	Compare post-BL Urine Blood (Dipstick) toxicity grade to BL Urine Blood (Dipstick) toxicity grade. If post-BL toxicity is greater than BL toxicity, then treatment-emergent
No	-	Yes	No	Treatment-emergent. Use post-BL Urine Blood (Dipstick) toxicity grade.
No	-	No	-	Do not count subject in the denominator for "Urine RBC (Hematuria, Quantitative or Dipstick)"

BL = Baseline. Quant = Quantitative. "-" means any value can be present (or it can be missing), as it does not affect the classification

16) Concomitant nonstudy-drug ARV medications for all B/F/TAF analysis (ie, ARV medications other than study drug that are taken while receiving study drug B/F/TAF) will be flagged in "Nonstudy-Drug Antiviral Medication" listing. The logic to define concomitant nonstudy-drug ARV is similar to concomitant non-ARV Medications (see details in Section 7.4.2)

17) Lipid modifying medication analyses for All B/F/TAF analysis:

    Lipid modifying medication is defined to be the concomitant medication with ATC2 term = "LIPID MODIFYING AGENTS" and CMDECOD contains wording of "STATIN" in the ADCM dataset.

    Subjects who took lipid-modifying medications at the first dose of B/F/TAF (including both phases) refer to the subjects who use of the lipid-modifying agents at study day 1 of all B/F/TAF analysis. More specifically, subjects with "Lipid Modifying Agent Use at the first dose of B/F/TAF" include those subjects in All B/F/TAF Analysis Set with: 1) any selected CM record with the start date ≤ the first dose date of B/F/TAF (including both phases), and 2) the end date of the selected CM record is ongoing or the end date of the selected CM record ≥ the first dose date of B/F/TAF (including both phases).

    Subjects who initiated lipid-modifying medications while subject receiving B/F/TAF includes the following subjects in the All B/F/TAF Analysis Set: (1) for subjects who permanently discontinued study drug with any selected CM record started after the first dose date of B/F/TAF (including both phases) and on and prior to the last dose of B/F/TAF (including both phases); 2) for subjects who meet criteria (1) above, if they took lipid modification medications before the first dose of B/F/TAF (including both phases), they will not be considered initiated lipid modifications while receiving B/F/TAF for the All B/F/TAF analysis.

For lipid-modifying medications with the start date completely unknown, we assume the start date is on or before the first dose date of B/F/TAF (including both phases), lipid-modifying medication was considered as being taken at the first dose of B/F/TAF (including both phases) if the end date is not prior to the first dose date B/F/TAF (including both phases) (ie, the end date is on or after the first dose date of B/F/TAF (including both phases), completely unknown, or ongoing).

18) For figures, if at a visit where n (sample size) for any treatment group ≤ 5, data for that treatment group will not be displayed at the visit in figure (except the Kaplan-Meier figure), but all data will be included in the corresponding table summary.

19) HIV/HBV and HIV/HCV Coinfection:

- The following table presents the HBV and HCV tests with all possible values. Values that have an asterisk after them denote a "positive" (or "quantifiable" for HBV DNA and HCV RNA) result while all others denote a "negative" result.

Label	LBTESTCD	LBTEST	Possible Values
HBsAg	CNT550	Hep B Surface Ag2	"Positive"*, "Positive, Confirmed"*,"Negative"
HBsAg	ATT2	Hep. B Surf. Ag Qual(-70)-PS	"Repeat reactive, confirmed"*, "Repeat Reactive Unconfirmed", "Non-Reactive"
HBsAb	CNT353	anti-Hep B Surface Ag2 Qual	"Positive"*, "Negative"
HBcAb	CNT68	Hepatitis B Core Total	"Positive"*, "Negative"
HBV DNA	GET1883	HBV DNA CAP/CTM 2.0-EDTA-CL	"No HBV DNA detected", "<20 IU/mL HBV DNA detected", ">170000000"*, *NUMERICAL VALUE**
HCVAb	CNT350	Hepatitis C Virus Antibody	"Positive"*, "Indeterminate", "Negative"
HCV RNA	GET1881	HCV RNA CAP/CTM 2.0EDTA-CL	"No HCV RNA detected", "<15 IU/mL HCV RNA detected", *NUMERICAL VALUE**

- For baseline coinfection, for all B/F/TAF analysis, the baseline would be adjusted based on the first dose of B/F/TAF (including both phases), when considering the different laboratory tests, take the latest, non-missing record on or prior to the first dose date of B/F/TAF (including both phases) for each test (eg, HBsAg, HBsAb, HBcAb, and HBV DNA).

  — The baseline coinfection status will be one of the three values: Yes/No/Null

  — The following tables provide combinations of HBV and HCV tests and the corresponding baseline coinfection status

HBsAg	HBsAb	HBcAb	HBV DNA	Coinfection Status
Positive	-	-	-	Y
Negative	Positive	-	-	N
	Negative	Positive	Quantifiable	Y
			Not Quantifiable	N
			Missing	Null
		Negative	-	N
		Missing	Quantifiable	Null
			Not Quantifiable	N
			Missing	Null
	Missing	Positive	Quantifiable	Null
			Not Quantifiable	N
			Missing	Null
		Negative	-	N
		Missing	Quantifiable	Null
			Not Quantifiable	N
			Missing	Null
Missing	Positive	-	-	Null
	Negative	Positive	Quantifiable	Y
			Not Quantifiable	Null
			Missing	Null
		Negative	-	Null
		Missing	-	Null
	Missing	-	-	Null

HCVAb	HCV RNA	Coinfection Status
Positive	Quantifiable	Y
	Not Quantifiable	N
	Missing	Null
Negative	-	N
Missing	Quantifiable	Null
	Not Quantifiable	N
	Missing	Null

"-" means any value can be present, as it does not affect the classification

- For incident coinfection, all laboratory tests must share the same accession number and if any set of values meets the criteria, then the subject is considered to have incident coinfection

  — The incident coinfection status will be one of two values: Yes/Null

  — The following tables provide combinations of HBV and HCV tests that are considered "Y" for incident coinfection status (all others are considered Null)

HBsAg	HBsAb	HBcAb	HBV DNA	Coinfection Status
Positive	-	-	-	Y
Negative	Negative	Positive	Quantifiable	Y
Missing	Negative	Positive	Quantifiable	Y

HCVAb	HCV RNA	Coinfection Status
Positive*	-	Y
-	Quantifiable	Y

* Subjects with positive HCVAb postbaseline must also have negative or missing HCVAb at baseline in order to be considered as having incident HIV/HCV coinfection.
"-" means any value can be present, as it does not affect the classification

— For adverse events, the start date must be after the first dose date of B/F/TAF (including both phases) and on or prior to the last dose date

— For incomplete AE start dates, please follow the logic specified in Section 7.1.5.2, but modify the second criterion to read, "The month and year (or year) of the AE onset is the same as or before the month and year (or year) of the date of the last dose of study drug".

20) HBV DNA test codes: If the result of the lab test code GET1883 (HBV DNA CAP/CTM 2.0-EDTA-CL) is listed as ">170000000", then a reflexive test code GET1884 (HBV DNA CAP/CTM 2.0Dil-EDTA-CL) should be performed and will share the same accession number as the original GET1883 test. In this instance, use the result from GET1884 instead of GET1883 when determining HBV DNA.

21) Clarification for TEAE

The TEAE definitions will be applied to the randomized phase data and the extension phase data, separately. When randomized phase data are used, AEs onset date will be compared with the randomized phase first dose date and last dose date and premature discontinuation of study drug refers to study drug discontinuation in the randomized phase. An AE meeting the TEAE criteria will be considered as a TEAE in the randomized phase. When extension phase data are used, AEs onset date will be compared with the extension phase first dose date and last dose date and premature discontinuation of study drug refers to study drug discontinuation in the extension phase. AE meeting the TEAE criteria will be considered as a TEAE in the extension phase.

One AE will be included either in the randomized phase or extension phase, but not both, except that an AE is treatment-emergent in the randomized phase, but continuing into extension phase and leading to prematurely discontinuation of the study drug in the extension phase, which will be counted as treatment-emergent for both phases.

When an AE with missing onset date and according to the following rules for incomplete dates, an AE is treatment emergent in the extension phase, then the AE will be included in extension phase and considered treatment emergent in extension phase only.

Events with Missing Onset Day and/or Month

An AE is treatment emergent if the following 3 criteria are met:

1) The month and year (or year) of onset date is the same as or after the month and year (or year) of the first dose of study drug, and
2) The month and year (or year) of the onset date is the same as or before the month and year (or year) of the 30th day after the date of the last dose of study drug, and
3) End date is as follows:
    a. The (complete) end date is on or after the first dose date, or
    b. The month and year (or year) of end date is the same or after the month and year (or year) of the first dose of study drug, or
    c. End date is completely missing

Events with Completely Missing Onset Date

An AE with a completely missing onset date is defined as TEAE if end date meets any of the criteria specified in 3) above.

22) LDL: Conversions between 2nd and 3rd generations

LDL was analyzed by 2 different assays in the study: 2nd generation (including RCT2394, RCT2312, and RCT2811) and 3rd generation (RCT3870). Samples collected at earlier visits were analyzed using LDL 2nd generation assay. Samples collected at later visits were analyzed using LDL 3rd generation assay. The conversion formulas are as follow:

2nd Gen (mmol/L) = (3rd Gen - 0.0626)/0.882

3rd Gen (mmol/L) = (0.882 x 2nd Gen) + 0.0626

For this analysis, since LDL samples were analyzed by 2nd generation assay at Baseline, we only requested conversion from 3rd generation to 2nd generation.

For the analysis of change from baseline in fasting direct LDL: the sample analyzed by LDL 3rd generation assay will be converted to 2nd generation as a new record with test codes of LIP.LDL.00.02 in raw data. During ADaM stage, a derived parameter code (FLDL2) for "Fasting LDL Cholesterol 2ND GEN Combined" will be generated to pool the records from both original (including test codes RCT2394, RCT2312, and RCT2811) and converted (LIP.LDL.00.02) 2nd generation results to calculate the change from baseline in fasting direct LDL.

For the analysis of toxicity grade for fasting direct LDL: toxicity grade will be based on the Gilead grading results (ie, toxgrg) from original values before conversion. In another words, during ADaM stage, a derived parameter code (FLDLTOX) for "Fasting LDL Cholesterol for Toxicity" will be generated to pool the records from 2nd generation (including RCT2394, RCT2312, and RCT2811) and 3rd generation (ie, RCT3870) to derive treatment-emergent toxicity grades, maximum postbaseline toxicity grades, etc.

23) Correction for Serum creatinine and eGFR (corrected)

1. Calibration lot changed on 01JUL2018 local time.
2. For samples collected on or after 01JUL2018, please use the inverse conversion formula in the below table.
3. The correction is based on unit of umol/L, after correction by regular regression, covert to mg/dL by multiplying 0.0113.

Regional Lab Center	Accession Number	Regular Regression for Correction (umol/L)	Inverse Conversion Formula (umol/L)
Indy	start with 65	Y=1.002*X+1.77	Y=(X-1.77)/1.002
GVA	start with 62 or 63	Y=1.025*X+2.62	Y=(X-2.62)/1.025
SHANGHAI	start with 67	Y=0.971*X+5.42	Y=(X-5.42)/0.971
SINGAPORE	start with 64 or 66	Y=1.009*X-1.42	Y=(X+1.42)/1.009
JAPAN	start with 68	Y=1.033*X+7.25	Y=(X-7.25)/1.033

Recalculate eGFR using the corrected serum creatinine, using the following formula:

eGFRCG (mL/min) = [(140 – age (yrs)) × weight (kg) × (0.85 if female)] / (SCr (mg/dL) × 72), where weight is total body mass in kilograms, and SCr is serum creatinine.

Here age refers to the age at the sample collection date. Use the derived visit to align serum creatinine and weight. For multiple records, choose the one with analysis flag

For this analysis, since serum creatinine samples were analyzed before lot change at Baseline, we only requested conversion to the results with previous lot for serum creatine and eGFR.

For the analysis of change from baseline in serum creatine and eGFR: the sample analyzed by updated calibration lot will be converted to the results assuming old calibration lot used as a new record. During ADaM stage, a derived parameter code (SCREA2) for "Serum Creatine before and after calibration change combined" and (EGFR2) for "eGFR before and after calibration change combined" will be generated to pool the records from both original and converted results to calculate the change from baseline in serum creatine and eGFR.

For the analysis of toxicity grade for serum creatine and eGFR: toxicity grade will be based on the Gilead grading results (ie, toxgrg) from original values before conversion. In another words, during ADaM stage, derived parameter codes (SCREATOX and EGFRTOX) for "Serum Creatine for Toxicity" and "eGFR for Toxicity" will be generated to pool the records from after calibration change and before calibration change to derive treatment-emergent toxicity grades, maximum postbaseline toxicity grades, etc.

24) Study and/or study drug discontinuations due to COVID-19

a) Study Drug Discontinuation

- Run NLP algorithm on the comment field from Study Drug Completion eCRF, checking for "COVID-19" text
- In COCOVID19 data set if COFORM = "Study Drug Completion" , then subject discontinued study drug due to COVID-19
- If study drug discontinued due to an AE, check if corresponding AE flagged as a COVID-19

b) Study Discontinuation

- Run NLP algorithm on the comment field from general comments for "COVID-19" text
- In COCOVID19 data set if COFORM = "Study Completion", then subject discontinued study due to COVID-19

If study discontinued due to an AE, check if corresponding AE flagged as a COVID-19

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ELECTRONIC SIGNATURES

Signed by	Meaning of Signature	Server Date (dd-MMM-yyyy hh:mm:ss)
PPD	Biostatistics eSigned	22-Sep-2021 19:58:08
PPD	Project Team Leader eSigned	22-Sep-2021 21:24:30