STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of Switching from a Regimen of Dolutegravir and ABC/3TC, or a Fixed Dose Combination (FDC) of ABC/DTG/3TC to a FDC of GS-9883/F/TAF in HIV-1 Infected Subjects who are Virologically Suppressed
Name of Test Drug:	Bictegavir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF; GS-9883/F/TAF)
Study Number:	GS-US-380-1844
Protocol Version (Date):	Amendment 2 (19 October 2016)
Analysis Type:	Week 48 Interim Analysis
Analysis Plan Version:	Version 1.0
Analysis Plan Date:	08 May 2017
Analysis Plan Author(s):	PPD

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LIST OF ABBREVIATIONS

3TC	lamivudine
ABC	abacavir
ABC/DTG/3TC	fixed dose combination of abacavir (ABC) 600 mg / dolutegravir (DTG) 50 mg / lamivudine (3TC) 300 mg
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
BMD	bone mineral density
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
DSPH	Drug Safety and Public Health
DTG	dolutegravir, tivicay
DXA	dual energy x-ray absorptiometry
ECG	electrocardiogram
eCRF	electronic case report form
eGFR	estimated glomerular filtration rate
$eGFR_{(CG)}$	estimated glomerular filtration rate using Cockcroft-Gault formula
FAS	full analysis set
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.
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
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

STB	stribild
TAF	tenofovir alafenamide
TFL	tables, figures, and listings
TFV	tenofovir
TSH	thyroid stimulating hormone; thyrotropin
ULN	upper limit of normal
WHO	World Health Organization

PHARMACOKINETIC ABBREVIATIONS

AUC_{last}	area under the concentration versus time curve from time zero to the last quantifiable concentration
AUC_{tau}	area under the concentration versus time curve over the dosing interval
C_{last}	last observed quantifiable concentration of the drug in plasma
C_{max}	maximum observed concentration of drug in plasma
C_{tau}	observed drug concentration at the end of the dosing interval
CLss/F	apparent oral clearance after administration of the drug: at steady state: CLss/F = Dose/AUC_{tau} , where "Dose" is the dose of the drug
LAMBDAZ(λz)	terminal elimination rate constant, estimated by linear regression of the terminal elimination phase of the plasma concentration of drug versus time curve
THALF ($t_{1/2}$)	estimate of the terminal elimination half-life of the drug in plasma, calculated by dividing the natural log of 2 by the terminal elimination rate constant (λz)
T_{last}	time (observed time point) of C_{last}
T_{max}	time (observed time point) of C_{max}
Vz/F	apparent volume of distribution of the drug

1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical analysis methods and data presentations to be used in tables, figures, and listings (TFLs) of the Week 48 interim analysis for Study GS-US-380-1844, which will be performed when all subjects have completed their Week 48 visit or prematurely discontinued from the study drug. This SAP is based on the study protocol amendment 2 dated 19 October 2016 and the electronic case report form (eCRF). The SAP will be finalized before database finalization for the interim analysis. Any changes made after the finalization of the SAP will be documented in the clinical study report (CSR).

1.1. Study Objectives

The primary objective of this study is:

- To evaluate the efficacy of switching from a regimen of DTG and ABC/3TC or a fixed dose combination (FDC) of abacavir /dolutegravir /lamivudine (ABC/DTG/3TC) to a FDC of bictegravir (GS-9883; BIC; B)/ emtricitabine (FTC; F) / tenofovir alafenamide (TAF) versus continuing DTG and ABC/3TC as the FDC ABC/DTG/3TC in virologically suppressed HIV-infected subjects as determined by the proportion of subjects with HIV-1 ribonucleic acid (RNA) ≥ 50 copies/mL at Week 48

The secondary objectives of this study are:

- To evaluate the safety and tolerability of the two treatment groups through Week 48
- To evaluate the bone safety of the two treatment groups as determined by the percentage change from baseline in hip and spine bone mineral density (BMD) through Week 48

1.2. Study Design

Design Configuration and Subject Population

GS-US-380-1844 is a randomized, double-blinded, multicenter, active-controlled study to evaluate the safety and efficacy of switching to a FDC of B/F/TAF tablet versus continuing DTG and ABC/3TC as the FDC ABC/DTG/3TC in HIV- infected subjects who are virologically suppressed.

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 FDC of abacavir 600 mg/ dolutegravir 50 mg/lamivudine 300 mg (ABC/DTG/3TC) administered orally, once daily, without regard to food (n = 260)
- **Treatment Group 2:** FDC of abacavir 600 mg/dolutegravir 50 mg/ lamivudine 300 mg (ABC/DTG/3TC) + 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 = 260)

Key Eligibility Criteria

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

- Currently receiving an antiretroviral regimen of DTG + ABC/3TC, or ABC/DTG/3TC FDC for ≥ 3 months prior to screening

- Currently on a stable regimen for ≥ 3 months preceding the Screening visit with documented plasma HIV-1 RNA < 50 copies/mL for ≥ 3 months preceding the Screening visit (or undetectable HIV-1 RNA level according to the local assay being used if the limit of detection is ≥ 50 copies/mL).

  — Prior changes in antiretroviral regimen are only allowed due to tolerability issues or for regimen simplification. Unconfirmed virologic elevations of ≥ 50 copies/mL (transient detectable viremia, or "blip") prior to screening are acceptable. If the lower limit of detection of the local HIV-1 RNA assay is <50 copies/mL (eg, < 20 copies/mL), the plasma HIV-1 RNA level cannot exceed 50 copies/mL on two consecutive HIV-1 RNA tests.

- Estimated GFR ≥ 50 mL/min according to the Cockcroft-Gault formula for creatinine clearance

- No chronic Hepatitis B Virus (HBV) infection, as determined by either

  — Positive HBV surface antigen (HBsAg) and negative HBV surface antibody (HBsAb), regardless of HBV core antibody (HBcAb) status, at the screening visit

  — Positive HBV core antibody and negative HBV surface antibody, regardless of HBV surface antigen status, at the screening visit

Study Periods / Phases

Subjects will be treated for at least 48 weeks during the blinded treatment phase. After Week 48, 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 48 visit and Gilead Sciences Inc. (Gilead) completes the Week 48 analysis, all subjects will return to the clinic (preferable within 30 days) for an End of Blinded Treatment Visit. At the End of Blinded Treatment Visit, if safety and efficacy of B/F/TAF are demonstrated following review of unblinded data, subjects in a country where B/F/TAF FDC is not available will be given the option to receive B/F/TAF FDC in an open-label (OL) extension phase for up to 96 weeks, or 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 up to 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 30 days 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 48 weeks. Following the Day 1 visit, subjects will return for study visits at Weeks 4, 8, and 12, and then every 12 weeks through Week 48. After Week 48, all subjects will continue to take their blinded study drugs and attend study visits every 12 weeks until the End of Blinded Treatment Visit.

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. Laboratory analyses (hematology, chemistry, and urinalysis), HIV-1 RNA, CD4+ cell count, and complete or symptom-directed physical examinations will be performed at the Screening, Day 1 and all subsequent study visits.

In addition, blood will be collected and stored for possible evaluation of markers of inflammation and immune activation, which may include but not limited to: cystatin C, IL-6, hs-CRP, d-dimer, sCD14, and sCD163. Platelet function evaluations may also be assessed, including but not limited to soluble glycoprotein VI (sGPVI), P-selectin, and soluble CD40 ligand. Urine will be collected for evaluations of renal function including urine albumin, urine creatinine, urine protein, retinol binding protein (RBP), and beta-2 microglobulin.

For all subjects on study drug, except subjects located in Germany, dual energy x-ray absorptiometry (DXA) scans will be performed prior to or within 24 hours of the Day 1 Visit, and then at Weeks 24, 48 and at the End of Blinded Treatment Visit or Early Study Drug Discontinuation Visit (blinded treatment phase only), if > 12 weeks since last scan. DXA scan results will be provided to study sites when available.

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

More details for study procedure could be found in Appendix 1.

Pharmacokinetics

An intensive pharmacokinetic (PK) substudy will be performed at the Weeks 4 or 8 visits in a subset of subjects (target n = 30) at study sites able to conduct this testing.

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).

Site and/or Stratum Enrollment Limits

Approximately 100 study sites in North America, Europe, and Asia Pacific participated. There was no enrollment limit for individual sites.

Study Duration

The randomized, double-blind phase of this study is at least 48 weeks in duration.

1.3. Sample Size and Power

A total of approximately 520 HIV- infected subjects, randomized in a 1:1 ratio to 2 treatment groups (260 subjects per treatment group), achieves at least 90% power to detect a non-inferiority margin of 4% difference in the percentage of subjects with HIV-1 RNA ≥ 50 copies/mL at Week 48 between the 2 treatment groups. For the sample size and power computation, it is assumed that both treatment groups have 2% of subjects with HIV-1 RNA ≥ 50 copies/mL at Week 48 (based on the historical Gilead Genvoya (GEN; E/C/F/TAF) and stribild [STB] studies), that the non-inferiority margin is 4%, 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 will be conducted after all subjects either complete their Week 48 visit or prematurely discontinue from the study drug.

This statistical analysis plan describes the analysis plan for the Week 48 interim analysis, the primary analysis of this study.

2.3. Final Analysis

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

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

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

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

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.

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 study drug refers to premature discontinuation of study drug or completion of study drug.

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

3.1.2. Full Analysis Set

The **Full Analysis Set (FAS)** will include all subjects who (1) are randomized into the study and (2) have received at least 1 dose of study drug. Subjects will be grouped according to the treatment to which they were randomized. For the FAS, all efficacy data, including data collected after the last dose of study drug, will be included, unless specified otherwise. This is the primary analysis set for efficacy analyses.

3.1.3. Per Protocol Analysis Set

The Week 48 **Per Protocol (PP) Analysis Set** will include all subjects who (1) are randomized into the study, (2) have received at least 1 dose of study drug, and (3) have not committed any major protocol violation, including the violation of key entry criteria. Subjects will be grouped according to the treatment they actually received. For the PP analysis, efficacy data up to 1 day after permanent discontinuation of study drug will be included. The Week 48 PP analysis set is the secondary analysis set for efficacy analysis.

Subjects meeting any of the following criteria will be excluded from the Week 48 PP analysis set:

- Subjects who do not have on-treatment HIV-1 RNA in the Week 48 analysis window, except when missing is due to discontinuation of study drug for lack of efficacy. (Note: lack of efficacy is defined as having the check-box for Lack of Efficacy marked as the reason for premature study drug discontinuation in the "Blinded Treatment" study phase on the study drug completion eCRF page; Table 3-1).

Table 3-1. Subjects Excluded from Week 48 PP Analysis Set Due to Premature Discontinuation of Study Drug and/or Missing HIV-1 RNA Assessment in Week 48 Analysis Window

Discontinuation from Study Drug prior to or on the Upper Bound of Week 48 Analysis Window		HIV-1 RNA Data on Randomized Treatment Available in Week 48 Analysis Window	
		Yes	No
Yes	Due to Lack of Efficacy	+	+
	Due to Other Reasons	+	-
No		+	-

+ = Inclusion of Subjects in Week 48 PP analysis set; - = Exclusion of Subjects in Week 48 PP analysis set.

- Subjects who do not meet the inclusion criterion of receiving an antiretroviral regimen of DTG + ABC/3TC, or ABC/DTG/3TC FDC for ≥ 3 months prior to the screening visit

- Subjects who do not meet the inclusion criterion of being on a stable regimen for ≥ 3 months preceding the screening visit with documented plasma HIV-1 RNA < 50 copies/mL for ≥ 3 months preceding the Screening visit (or undetectable HIV-1 RNA level according to the local assay being used if the limit of detection is ≥ 50 copies/mL).

- Subjects who do not meet the inclusion criterion of having no documented or suspected resistance to FTC, TFV, DTG, ABC or 3TC including, but not limited, to the reverse transcriptase resistance mutations K65R and M184V/I

- Subjects who do not meet the inclusion criterion of having HIV RNA < 50 copies/mL at the screening visit

- Subjects who meet the exclusion criterion for receiving ongoing therapy with any of the medications listed in the table in protocol Section 4.3 including drugs not to be used with BIC, FTC, TAF, DTG, ABC, and 3TC

- Nonadherence to study drug: subjects with adherence rate for active study drug up to the Week 48 Visit below the 2.5th percentile

3.1.4. Safety Analysis Set

The **Safety Analysis Set** will include all subjects who (1) are randomized into the study and (2) have received at least 1 dose of study drug. All the data collected up to 30 days after permanent discontinuation of the study drug will be included in the safety summaries, unless specified otherwise. Subjects will be grouped according to the treatment they actually received. This is the primary analysis set for safety analyses.

3.1.5. DXA Analysis Set

3.1.5.1. Hip DXA Analysis Set

The **Hip DXA Analysis Set** will include all subjects who (1) are randomized into the study, (2) have received at least 1 dose of study drug, and (3) have nonmissing baseline hip BMD values. Subjects will be grouped according to the treatment they actually received.

3.1.5.2. Spine DXA Analysis Set

The **Spine DXA Analysis Set** will include all subjects who (1) are randomized into the study, (2) have received at least 1 dose of study drug, and (3) have nonmissing baseline spine BMD values. Subjects will be grouped according to the treatment they actually received.

For the hip DXA and spine DXA analysis sets, all data including data collected after the last dose of study drug will be used for analysis, unless specified otherwise.

3.1.6. Pharmacokinetic Analysis Set

The **PK Analysis Set** will include all subjects who (1) are randomized into the study, (2) have received at least 1 dose of active B/F/TAF, and (3) have at least 1 nonmissing PK concentration value for any analyte of interest reported by the PK lab. The PK analysis set will be used for general PK analyses.

3.1.7. Pharmacokinetic Substudy Analysis Set

The **PK Substudy Analysis Set** will include all subjects who (1) are randomized into the study, (2) are enrolled into the PK Substudy, (3) have received at least 1 dose of active B/F/TAF, and (4) have at least 1 nonmissing intensive PK concentration value for any analyte of interest reported by the PK lab. The PK substudy analysis set will be used for intensive PK analyses.

3.2. Subject Grouping

For analyses based on the All Randomized Analysis Set or the FAS, subjects will be grouped by randomized treatment. For other analyses, subjects will be grouped by actual treatment received. 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.

3.3. Strata and Covariates

There is no stratification for randomization.

3.4. Examination of Subject Subgroups

3.4.1. Subject Subgroups for Efficacy Analyses

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} will be analyzed for the following subject subgroups (also see Section 6.2.2.2 for details):

- Age (years): (a) < 50 and (b) ≥ 50
- Sex: (a) male and (b) female
- Race: (a) black and (b) nonblack
- Region: (a) US and (b) Ex-US
- Study drug adherence (%): (a) < 95 and (b) ≥ 95 (based on adherence up to Week 48 visit)

3.4.2. Subject Subgroups for Safety Analyses

Incidence of all treatment-emergent AEs (TEAEs) will be analyzed for the following subject subgroups (also see Section 7.1.5):

- Age (years): (a) < 50 and (b) ≥ 50
- Sex: (a) male and (b) female
- Race: (a) black and (b) nonblack
- Region: (a) US and (b) Ex-US

Selected safety endpoints may be analyzed for the following subject subgroups (see Section 9.1 for details):

- 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

The noninferiority evaluation of the proportion of subjects with HIV-1 RNA ≥ 50 copies/mL at Week 48 as determined by US FDA-defined snapshot algorithm was the prespecified primary comparison. However, 2 interim IDMC analyses were performed prior to the analysis for the primary endpoint and an alpha penalty of 0.00001 was applied for each interim IDMC meeting. Therefore, the alpha level for the primary endpoint (ie, the proportion of subjects with HIV-1 RNA ≥ 50 copies/mL at Week 48 as determined by the US FDA-defined snapshot algorithm) was adjusted to 0.04998 (corresponding to 95.002% confidence interval [CI]) using both the FAS and the Week 48 PP analysis set. The alpha level for the key secondary efficacy endpoint, the proportion of subjects with HIV-1 RNA < 50 copies/mL at Week 48 as defined by the US FDA defined snapshot algorithm, will be also adjusted to 0.04998 (corresponding to 95.002% CI) to be conservative.

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 adverse event (AE) onset is described in Section 7.1.4.2, and for concomitant non-ARV medications in Section 7.5.2.

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 Deoxyribonucleic Acid (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.

Natural logarithmic transformations will be used for analyzing concentrations and PK parameters in intensive plasma samples. Concentration values (including intensive, trough, postdose, anytime PK concentration, etc) that are below the lower limit of quantitation (BLQ) will be presented as "BLQ" in the concentration listing. Intensive PK concentration values that are BLQ will be treated as 0 at predose time points, and one-half the value of the lower limit of quantitation (LLOQ) at postdose time points for summary purposes. . Other PK concentration values (including trough, predose, postdose, anytime PK concentration) that are BLQ will be treated as one-half of the LLOQ.

The following conventions will be used for the presentation of order statistics and summary statistics for intensive PK concentration:

- If at least 1 subject has a concentration value of BLQ for the time point, the minimum value will be displayed as "BLQ."

- If more than 25% of the subjects have a concentration value of BLQ for a given time point, the minimum and Q1 values will be displayed as "BLQ."

- If more than 50% of the subjects have a concentration value of BLQ for a given time point, the minimum, Q1, and median values will be displayed as "BLQ."

- If more than 75% of the subjects have a concentration value of BLQ for a given time point, the minimum, Q1, median, and Q3 values will be displayed as "BLQ."

- If all subjects have concentration values of BLQ for a given time point, all order statistics (minimum, Q1, median, Q3, and maximum) and summary statistics will be displayed as "BLQ."

3.8. Analysis Windows

3.8.1. Definition of Study Day

Study Day 1 is defined as the day when the first dose of study drug (ie, *B/F/TAF or Placebo,* or *ABC/DTG/3TC or Placebo*) was taken, as recorded on the Study Drug Administration eCRF form.

Study Days are calculated relative to Study Day 1. For events that occurred on or after the Study Day 1 date, study days are calculated as (visit date minus Study Day 1 plus 1). For events that occurred prior to Study Day 1, study days are calculated as (visit date minus Study Day 1).

Last Dose Date is the latest of the blinded study drug end dates recorded on the Study Drug Administration eCRF form with "Permanently Withdrawn" box checked for subjects who prematurely discontinued or completed study drug in the "Blinded Treatment" study phase according to the Study Drug Completion-Blinded eCRF.

If the date of last dose is missing (eg, only year of last dose is known or completely missing due to lost to follow-up) for subjects who prematurely discontinued or completed blinded study drug at the data cut date, the latest of the study drug start dates and end dates, the clinical visit dates, and the laboratory visit dates, excluding the date of 30-day follow-up visit, 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.

Last Study Date is the latest of the study drug start dates and end dates, the clinic visit dates, and the laboratory visit dates, including the 30-day follow-up visit date, for subjects who prematurely discontinued study or who completed study according to the Study Completion eCRF.

Baseline value is defined as the last value obtained on or prior to Study Day 1 for all assessments, except for DXA BMD. The baseline value for DXA BMD is defined as the last value obtained on or prior to Study Day 14.

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 analysis windows.

The analysis windows for HIV-1 RNA, CD4+ cell count, CD4 %, hematology, chemistry, urinalysis, urine pregnancy laboratory tests, $eGFR_{CG}$, vital signs, and weight are presented in Table 3-2.

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

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 K (K is every 12 weeks after previous visit)	K*7	(K-6)*7+1	(K+6)*7

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) are presented in Table 3-3.

Table 3-3. Analysis Windows for Metabolic Assessments

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 K (K is every 24 weeks after previous visit)	K*7	(K-12)*7+1	(K+12)*7

The analysis windows for thyroid stimulating hormone (TSH; thyrotropin), and renal function (including: urine albumin, urine creatinine, urine protein, urine RBP, and urine beta-2 microglobulin, and derived ratios) are presented in Table 3-4.

Table 3-4. Analysis Windows for TSH and Renal Function

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 K (K is every 24 weeks after previous visit)	K*7	(K-12)*7+1	(K+12)*7

The analysis windows for HBV and HCV Serology (including HBsAb, HBsAg, hepatitis B e-antigen [HBeAg], hepatitis B e-antibody [HBeAb], HBcAb, and HCV antibody [HCVAb]), HBV DNA and HCV RNA assessments are presented in Table 3-5.

Table 3-5. Analysis Windows for HBV and HCV Serology, HBV DNA and HCV RNA Assessments

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

The analysis windows for safety electrocardiogram (ECG) are presented in Table 3-6.

Table 3-6. Analysis Windows for Safety ECG

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 K (K is every 48 weeks after previous visit)	K*7	(K-24)*7+1	(K+24)*7

The analysis windows for DXA BMD are presented in Table 3-7.

Table 3-7. Analysis Windows for DXA BMD

Visit ID	Nominal Day	Lower Limit	Upper Limit
Baseline			14
Week 24	168	15	252
Week 48	336	253	420
Post Week 48	NA	421	NA

Note: The baseline value of DXA BMD is defined as the last value obtained on or prior to Study Day 14.
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 BMD data, 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 BMD data), 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-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

The number and percentage of subjects randomized at each region, country, and investigator will be summarized by treatment group and overall using the safety analysis set. The region definition is provided in Appendix 3. The denominator for this calculation will be the number of subjects in the safety analysis set.

4.1.2. Subject Disposition

The summary of subject disposition will be provided by treatment group and overall for all screened subjects. This summary will include the number of subjects screened, screen failure subjects who were not randomized, subjects who met all eligibility criteria and were not randomized, 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:

- Still on study drug up to the data cut date
- Prematurely discontinuing study drug prior to the data cut date (with summary of reasons for discontinuing study drug)
- Still on study up to the data cut date
- Prematurely discontinuing from study prior to the data cut date (with summary of reasons for discontinuing study).

The denominator for the percentages of subjects in each category will be the number of subjects in the safety analysis set.

No inferential statistics will be generated. A data listing of reasons for premature study drug/study discontinuation will be provided.

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 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). For the calculation of the duration of exposure to study drug, the data cut date will be used to impute the last dose date for subjects who have not permanently discontinued study drug at the time of the data cut date.

Duration of exposure to study drug will be summarized using descriptive statistics (n, 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), etc.

Summaries will be provided by treatment group for subjects in the safety analysis set. No inferential statistics will be provided.

Time to permanent discontinuation of study drug will be analyzed using the Kaplan-Meier method by treatment group based on the safety analysis set. The log rank test will be used to compare the difference in study drug exposure between the 2 treatment groups. Subjects who are still on the randomized study drug will be censored on the imputed last dose date as defined in this section. A plot of KM estimates for the time to premature discontinuation of study drug by treatment group will be generated.

4.2.2. Adherence to Study Drug Regimen

Study drug regimen adherence will be computed based on pill counts for active drug only (eg, study drug regimen in Treatment Group 1 includes 1 study drug: *B/F/TAF active*. Study drug regimen in Treatment Group 2 includes 1 study drug: *ABC/DTG/3TC active*). 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.

Adherence up to the data cut date will be calculated using all data from the entire dosing period up to the date of permanent discontinuation of the study drug for subjects who prematurely discontinued study drug, or completed study drug, or using all data available for subjects who are ongoing on study drug.

Adherence up to Week 48 visit will also be calculated using all data from the entire dosing period up to the date of permanent discontinuation of the study drug for subjects who prematurely discontinued study drug, or completed study drug, or the Week 48 study drug dispensing date, whichever occurs earliest.

Descriptive statistics for adherence up to the data cut date and adherence up to Week 48 visit for a study drug regimen (n, 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 and have calculable adherence during the study in the safety 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.

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 subject characteristics will be provided for the safety analysis set.

For categorical data, the Cochran-Mantel-Haenszel (CMH) test (ie, general association statistic for nominal data) will be used to compare the 2 treatment groups. For continuous data, the 2-sided Wilcoxon rank sum test will be used to compare the 2 treatment groups.

5.2. Baseline Disease Characteristics

The following baseline disease characteristics will be summarized by treatment group and overall using descriptive statistics:

- HIV-1 RNA categories (copies/mL): (a) < 50, (b) ≥ 50
- 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)
- Medical history: diabetes mellitus (Yes/No), hypertension (Yes/No), cardiovascular disease (Yes/No), and hyperlipidemia (Yes/No) (see SAP Appendix 4 for details)
- HIV/HBV co-infection status (Yes/No/Missing, see Section 9.1 for definition)
- HIV/HCV co-infection status (Yes/No/Missing, see Section 9.2 for definition)
- Smoking status: (a) Never Smoker, (b) Former Smoker, and (c) Current Smoker (see SAP Appendix 6 for details)

For categorical data, the CMH test (general association statistic for nominal data, and row means scores differ statistic for ordinal data) will be used to compare the 2 treatment groups. For continuous data, the 2-sided Wilcoxon rank sum test will be used to compare the 2 treatment groups.

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

6.1. Primary Efficacy Endpoint

6.1.1. Definition of the 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 purpose.

6.1.2. US FDA-Defined Snapshot Algorithm

The analysis window at Week 48 is defined as from Study Day 295 to Study Day 378, inclusive. All HIV-1 RNA data collected on-treatment (ie, data collected up to 1 day after permanent discontinuation of study drug or all available data for subjects who were still on study drug) will be used in the US FDA-defined snapshot algorithm. Virologic outcome will be defined as the following categories:

- **HIV-1 RNA < 50 copies/mL:** this includes subjects who have the last available on-treatment HIV-1 RNA < 50 copies/mL in the Week 48 analysis window
- **HIV-1 RNA ≥ 50 copies/mL:** this includes subjects
  a) Who have the last available on-treatment HIV-1 RNA ≥ 50 copies/mL in the Week 48 analysis window, or
  b) Who do not have on-treatment HIV-1 RNA data in the Week 48 analysis window and
     1) Who discontinue study drug prior to or in the Week 48 analysis window due to lack of efficacy, or
     2) Who discontinue study drug prior to or in the Week 48 analysis window due to AE or death and have the last available on-treatment HIV-1 RNA ≥ 50 copies/mL, or
     3) Who discontinue study drug prior to or in the Week 48 analysis window due to reasons other than AE, death, or lack of efficacy and have the last available on-treatment HIV-1 RNA ≥ 50 copies/mL.
- **No Virologic Data in the Week 48 Window:** this includes subjects who do not have on-treatment HIV-1 RNA data in the Week 48 analysis window because of the following:
  a) Discontinuation of study drug prior to or in the Week 48 analysis window due to AE or death and the last available on-treatment HIV-1 RNA < 50 copies/mL, or
  b) Discontinuation of study drug prior to or in the Week 48 analysis window due to reasons other than AE, death, or lack of efficacy and the last available on-treatment HIV-1 RNA < 50 copies/mL or,
  c) Missing data during the window but on study drug.

The flowchart of the US FDA-defined snapshot algorithm is provided in Appendix 2.

The Week 48 virologic outcomes for the US FDA-defined snapshot algorithm will be listed.

Note, For switch trials, the US FDA-defined snapshot algorithm classifies subjects who discontinue study drug due to AE or death and have the last available on-treatment HIV-1 RNA value ≥ 50 copies/mL in the "HIV-1 RNA ≥ 50 copies/mL" category. For treatment naïve study population, these subjects will be classified in the "No Virologic Data in the Week 48 Window" category.

6.1.3. Statistical Hypothesis for the Primary Efficacy Endpoint

Null hypothesis: The B/F/TAF group (Treatment Group 1) is at least 4% higher than the ABC/DTG/3TC group (Treatment Group 2) with respect to the proportion of subjects with HIV-1 RNA ≥ 50 copies/mL as determined by the US FDA-defined snapshot algorithm) at Week 48.

Alternative hypothesis: The B/F/TAF group (Treatment Group 1) is less than 4% higher than the ABC/DTG/3TC group (Treatment Group 2) with respect to the proportion of subjects with HIV-1 RNA ≥ 50 copies/mL at Week 48.

6.1.4. Primary Analysis of the Primary Efficacy Endpoint

The analysis purpose of the primary efficacy endpoint is to assess the noninferiority of switching to B/F/TAF relative to continuing on ABC/DTG/3TC. Noninferiority will be assessed using a conventional 95% CI approach, with a noninferiority margin of 4%.

For each interim analyses performed for the IDMC at Weeks 12 and 24, an alpha of 0.00001 has been spent. Therefore, the significance level for the 2-sided test in the primary analysis at Week 48 will be 0.04998 (corresponding to 95.002% CI).

The point estimate of treatment difference (B/F/TAF group –ABC/DTG/3TC group) in the percentage of subjects with HIV-1 RNA ≥ 50 copies/mL and the associated 2-sided 95.002% CI will be constructed based on an unconditional exact method using 2 inverted 1-sided tests.

It will be concluded that B/F/TAF is noninferior to ABC/DTG/3TC if the upper bound of the 2-sided 95.002% CI of the difference between treatment groups (B/F/TAF group –ABC/DTG/3TC group) in the percentage of subjects with HIV-1 RNA ≥ 50 copies/mL is less than 4%.

The number and percentage of subjects with HIV-1 RNA < 50 copies/mL, HIV-1 RNA ≥ 50 copies/mL, and reasons for no virologic data at Week 48 will be summarized.

If noninferiority of B/F/TAF versus ABC/DTG/3TC is established, the same 95.002% CI used in evaluating noninferiority at Week 48 will be used to evaluate superiority. If the upper bound of the 95.002% CI is less than 0, then superiority of B/F/TAF over ABC/DTG/3TC is established. The 2-sided Fisher's exact test will also be used to assess superiority as a secondary assessment.

The FAS will be used for the primary efficacy endpoint analysis and the superiority evaluation.

6.1.5. Secondary Analysis of the Primary Efficacy Endpoint

A secondary analysis based on the Week 48 PP analysis set will also be performed to evaluate the robustness of the primary analysis of the primary endpoint. For this secondary analysis, 95.002% CI for the treatment difference in the primary efficacy endpoint will also be calculated based on an unconditional exact method using 2 inverted 1-sided tests.

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 Week 48 as determined by the US FDA-defined snapshot algorithm
- The change from baseline in CD4+ cell count at Week 48

The analyses for the secondary efficacy endpoints will be conducted using the FAS and the Week 48 PP analysis set, respectively.

6.2.2. Analysis of the Secondary Efficacy Endpoints

6.2.2.1. Analysis of the Proportion of Subjects with HIV-1 RNA < 50 copies/mL as Determined by US FDA-defined Snapshot Algorithm

The proportion of subjects with HIV-1 RNA < 50 copies/mL at Week 48 will also be analyzed by the US FDA-defined snapshot algorithm based on the FAS and Week 48 PP analysis set, respectively.

Proportion of subjects with HIV-1 RNA < 50 copies/mL at Week 48 as determined by US FDA-defined snapshot algorithm will be analyzed similarly to the primary efficacy endpoint. However, the noninferiority margin used for the proportion of subjects with HIV-1 RNA < 50 copies/mL will be 10%.

Similarly to the primary efficacy endpoint, noninferiority will be assessed using the conventional CI approach. The point estimate of treatment difference (B/F/TAFgroup -ABC/DTG/3TC group) in the percentage of subjects with HIV-1 RNA < 50 copies/mL and the associated 2-sided 95.002% CI will be constructed based on an unconditional exact method using 2 inverted 1-sided tests.

It will be concluded that B/F/TAF is noninferior to ABC/DTG/3TC if the lower bound of the 2-sided 95.002% CI of the difference between treatment groups (B/F/TAF group –ABC/DTG/3TC group) in the percentage of subjects with HIV-1 RNA < 50 copies/mL is greater than −10%.

The above analysis will be performed using both the FAS and the Week48 PP analysis set.

In addition, the following analyses will be performed using the FAS to evaluate the interaction between region and treatment to assess homogeneity of treatment effect across different regions.

A region is defined as multiple sites combined based on geographical locations (see Appendix 3 for region definition).

For each region, the difference in the proportion of subjects with HIV-1 RNA < 50 copies/mL between treatment groups and its 95% CI will be calculated based on an unconditional exact method using 2 inverted 1-sided tests.

The CMH analysis will be used to estimate the odds ratio and corresponding 95% CI for each region and overall. The homogeneity of the odds ratios across different regions will be tested using a Breslow-Day test and a corresponding p value will be reported.

6.2.2.2. Subgroup Analysis of the Proportion of Subjects with HIV-1 RNA < 50 copies/mLat Week48 as Determined by US FDA-defined Snapshot Algorithm

Since the proportion of subjects with HIV-1 RNA ≥ 50 copies/mL at Week 48 as determined by the US FDA-defined snapshot algorithm (primary endpoint) is expected to be very low (around 2%), the efficacy analysis by subgroup will be conducted by assessing the proportion of subjects with HIV-1 RNA < 50 copies/mL determined by the US FDA-defined snapshot algorithm at Week 48 (a secondary efficacy endpoint) within each subgroup specified in Section 3.4.1 based on the FAS.

For each level of subgroup factors, the proportion difference between treatment groups and the associated 2-sided 95% CIs will be computed based on an unconditional exact method using 2 inverted 1-sided tests.

Additionally, a logistic regression model will be performed which include subgroup, treatment, and treatment by subgroup interaction. The odds ratio and the associated 95% CI will be estimated within each subgroup. The homogeneity of the treatment effects between subgroups will be evaluated using a Wald test based on the interaction between treatment and the subgroup factor.

A forest plot of the treatment differences in HIV-1 RNA < 50 copies/mL (US FDA-defined snapshot algorithm) at Week 48 and their associated 95% CIs for each subgroup will be generated.

6.2.2.3. Analysis of CD4+ Cell Count

All CD4+ cell count will be summarized using observed, on-treatment data (ie, data collected up to 1 day after permanent discontinuation of study drug or all available data for subjects who were still on study drug) for subjects in the FAS.

The changes from baseline in CD4+ cell count at Week 48 will be summarized by treatment group using descriptive statistics. The differences in changes from baseline in CD4+ cell count between the 2 treatment groups and the associated 95% CI will be constructed using analysis of

variance (ANOVA) models, including treatment group as a fixed effect in the model. The change from baseline in CD4+ cell count will also be summarized at visits other than Week 48 by treatment group.

The change from baseline in CD4+ cell counts will also be analyzed based on the Week 48 PP analysis set.

The mean and 95% CI of change from baseline in CD4+ cell count over time will be plotted for the FAS.

In addition, the change from baseline in CD4+ cell counts with missing values imputed using the last observation carried forward (LOCF) method will be summarized at each visit based on the FAS. The algorithm for LOCF is as follows:

- If a value is missing in an analysis visit window, the missing value will be replaced with the last on-treatment value (ie, data collected up to 1 day after permanent discontinuation of study drug or all available data for subjects who were still on study drug) observed before the analysis visit window that has the missing value.
- Baseline values will be carried forward to impute the postbaseline value at a specific visit, if there is no non-missing postbaseline observation collected prior to that visit.

6.3. Tertiary Efficacy Endpoints

6.3.1. Definition of the Tertiary Efficacy Endpoints

PPD

6.3.2. Analysis of the Tertiary Efficacy Endpoints

6.3.2.1. Analysis of the Proportion of Subjects with HIV-1 RNA < 20 copies/mL at Week 48 as Determined by the US FDA-defined Snapshot Algorithm

PPD

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

PPD

PPD

[redacted]

6.3.2.3. Analysis of CD4%

PPD

[redacted]

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 for the subjects in the safety analysis set. All safety data collected up to 30 days after permanent discontinuation of study drug and all available data for subjects who were still on study drug will be summarized by treatment group, unless specified otherwise. All safety data will be included in data listings.

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. 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.

7.1.3. 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 SAE database from the Gilead Drug Safety and Public Health (DSPH) Department before data finalization.

7.1.4. Treatment-Emergent Adverse Events

7.1.4.1. 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.

7.1.4.2. 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.

7.1.5. 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. For other AEs described below, summaries will be provided by SOC, PT, and treatment group using the safety 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.

Summary of treatment-emergent AEs by SOC and PT will also be conducted for all subgroups listed in Section 3.4.2.

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

7.1.6. Additional Analysis of Adverse Events

7.1.6.1. 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.

7.1.6.2. Cardiovascular or Cerebrovascular Events

Preferred terms for cardiovascular or cerebrovascular events are from relevant Standardised MedDRA Query (SMQ). The selected PT listing was provided by Gilead DSPH and reviewed by Gilead medical monitors, which is the same PT listing used to search “Cardiovascular Disease” medical history (see details in Appendix 4).

The number and percentage of subjects with treatment-emergent cardiovascular or cerebrovascular events and serious cardiovascular or cerebrovascular events by PT will be summarized by treatment group based on the safety analysis set. Statistical comparisons of the subject incidence rates between the 2 treatment groups will be performed using the Fisher's exact test. A data listing of cardiovascular or cerebrovascular events will be provided.

7.1.6.3. Hepatic Events

Preferred terms for 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 DSPH and reviewed by Gilead medical monitors (see details in Appendix 5).

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 safety analysis set. Statistical comparisons of the subject incidence rates between the 2 treatment groups will be performed using the Fisher's exact test. A data listing of hepatic events 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 Safety 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. 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.

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 non-fasting lipid results (or lipid results without 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 or the last available date for subjects who were still on study drug at the time of an interim analysis. 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.

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.

Both urine RBC based on microscopic examination, labeled as Hematuria (Quantitative), and urine blood based on a dipstick, labeled as Hematuria (Dipstick), are assessed routinely and assigned a toxicity grade in this study. Urine RBC based on microscopic examination will be presented in laboratory toxicity summary tables and listings while urine blood based on a dipstick will be presented in the listings only.

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. P-values comparing the difference between the 2 treatment groups in baseline values and the change from baseline in metabolic assessment will be estimated from a 2-sided Wilcoxon rank sum test.

In addition, the number and percentage of subjects who took lipid modifying medications at study entry and initiated the medications during the study will be provided, respectively. Statistical comparisons of the subject incidence rates between the 2 treatment groups will be performed using Fisher's exact test.

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

A sensitivity analysis of fasting lipid tests will be performed by excluding subjects who took lipid modifying medications at study entry or initiated the medications during the study: baseline values, Week 48 values, and changes from baseline at Week 48 will be summarized by treatment group using descriptive statistics. Baseline and change from baseline at Week 48 will be compared between the 2 treatment groups using a 2-sided Wilcoxon rank sum test. Only subjects with both baseline and Week 48 postbaseline values will be included in the analysis.

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 × Upper limit of normal (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 safety 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, postbaseline, and change from baseline in AST, ALT, ALP, and total bilirubin will be summarized by treatment group and visit using descriptive statistics. Baseline and change from baseline will be compared between the 2 treatment groups using a 2-sided Wilcoxon rank sum test.

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. Baseline and change from baseline will be compared between the 2 treatment groups using a 2-sided Wilcoxon rank sum test.

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

7.2.5.2. Urine Retinol Binding Protein to Creatinine Ratio, Beta-2-Microglobulin to Creatinine Ratio, and Urine Creatinine

Baseline, postbaseline, change from baseline and percentage change from baseline in urine RBP to creatinine ratio and beta-2 microglobulin to creatinine ratio will be summarized by treatment group and visit using descriptive statistics. Baseline and percentage change from baseline will be compared between the 2 treatment groups using a 2-sided Wilcoxon rank sum test.

Median (Q1, Q3) percentage change from baseline in urine RBP to creatinine ratio and beta-2 microglobulin to creatinine ratio over time will be plotted by treatment group.

Baseline, postbaseline, and change from baseline in urine creatinine will be summarized by treatment group and visit using descriptive statistics. Baseline and change from baseline will be compared between the 2 treatment groups using a 2-sided Wilcoxon rank sum test.

7.2.5.3. Albuminuria by Quantitative Assessment

The baseline, postbaseline, changes from baseline, and percentage change from baseline in urine albumin to creatinine ratio (UACR) will be summarized by treatment group and visit using descriptive statistics. Baseline and percentage change from baseline will be compared between the 2 treatment groups using a 2-sided Wilcoxon rank sum test.

The number and percentage of subjects with UACR < 30 mg/g versus ≥ 30 mg/g will be summarized by baseline category at Weeks 24, 48, and based on the last on-treatment value (ie, data collected after the first dose date up to 1 day after the last dose date) {KDIGO Guideline Development Staff 2013}.

Median (Q1, Q3) percentage change from baseline in UACR over time will be plotted by treatment group.

7.3. Bone Safety Analyses

7.3.1. Bone Mineral Density

7.3.1.1 Percentage Change from Baseline in Hip and Spine Bone Mineral Density

The percentage change from baseline in hip BMD and spine BMD will be summarized by treatment group and visit using descriptive statistics for subjects in the hip and spine DXA analysis sets, respectively, and compared between the 2 treatment groups at each visit using ANOVA, which includes treatment as a fixed effect.

As a sensitivity analysis, missing values for hip BMD and spine BMD will be imputed using the LOCF imputation method for the analyses of percentage change from baseline. The algorithm for LOCF is as follows:

- If a value is missing in an analysis visit window, the missing value will be replaced with the last value observed before the analysis visit window that has the missing value.

- Baseline values will be carried forward to impute the postbaseline value at a specific visit, if there is no non-missing postbaseline observation collected prior to that visit.

Similar to the analysis of observed data, the percentage change from baseline in hip BMD and spine BMD by LOCF will also be analyzed using the hip and spine DXA substudy analysis sets.

Median (Q1, Q3) and mean (95% CI) of the percentage change from baseline in observed hip BMD and spine BMD over time will be plotted by treatment group. Listings of hip and spine DXA results will be provided.

7.3.1.2 Hip and Spine BMD Clinical Status

Analysis of hip and spine BMD clinical status will based on the observed BMD values (ie, missing will be excluded).

For each subject and each visit, the BMD clinical status will be defined for hip BMD and spine BMD as follows based on the t-score:

Table 7-1. Normal, Osteopenia, and Osteoporosis as Defined by T-score

Clinical Status	BMD T-score
Normal	T-score ≥ -1.0
Osteopenia	-2.5 ≤ T-score < -1.0
Osteoporosis	T-score < -2.5

The number and percentage of subjects in each BMD clinical status (normal, osteopenia, and osteoporosis) will be summarized by visit and by baseline clinical status for both hip and spine. The distribution of the BMD clinical status will be compared between the 2 treatment groups adjusting for baseline clinical status using rank analysis of covariance {LaVange 2008}.

7.3.1.3 Gradation of the Percentage Change in Hip, Femur Neck, and Spine BMD

For each subject and each visit, percentage change from baseline in spine BMD will be classified into 6 categories: ≥ 5% decrease, ≥ 3% to < 5% decrease, > 0% to < 3% decrease, ≥ 0% to < 3% increase, ≥ 3% to < 5% increase, and ≥ 5% increase. Similarly, the percentage change from baseline in Hip BMD and Femur Neck BMD will be classified into 6 categories: ≥ 7% decrease, ≥ 3% to < 7% decrease, > 0% to < 3% decrease, ≥ 0% to < 3% increase, ≥ 3% to < 7% increase, and ≥ 7% increase. The number and percentage of subjects in each category will be summarized by visit. The difference in the distribution of these categories between the treatment groups will be compared using a CMH test (row mean scores differ statistic).

In addition, the number and percentage of subjects with percentage change from baseline in each cumulative categories (ie, ≥ 5% decrease, ≥ 3% decrease, no decrease [≥ 0% increase], ≥ 3% increase, and ≥ 5% increase for Spine BMD; ≥ 7% decrease, ≥ 3% decrease, no decrease [≥ 0% increase], ≥ 3% increase, and ≥ 7% increase for Hip and Femur Neck BMD) will be compared between treatment groups using Fisher exact test based on the dichotomized response (eg, ≥ 5% decrease vs. < 5% decrease).

7.4. Body Weight, Height, and Vital Signs

Descriptive statistics will be provided by treatment group for vital signs and body weight as follows:

- 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.

7.5. Prior and Concomitant Medications

7.5.1. 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 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.

7.5.2. 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 name and drug code will be attached to the clinical database. Use of concomitant medications from Study Day 1 up to the date of last dose of study drug will be summarized (number and percentage of subjects) by treatment group, WHO drug class and preferred name. Multiple drug use (by preferred name) will be counted only once per subject. The summary will be sorted alphabetically by drug class and then by decreasing total frequency within a class.

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 safety analysis set. Subjects with any non-ARV concomitant medications will be listed. No inferential statistics will be provided.

7.6. Electrocardiogram Results

A shift table 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. 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.

7.7. 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.

7.8. Subject Subgroup for Safety Endpoints

Incidence of all treatment-emergent AEs will be repeated within each subgroup defined in Section 3.4.2 using the safety analysis set.

7.9. Changes From Protocol-Specified Safety Analyses

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

8. PHARMACOKINETIC ANALYSES

Pharmacokinetic parameters will be computed for all subjects in the PK substudy analysis set. Only analytes from B/F/TAF group presented in Table 8-1 will be analyzed and evaluated.

Table 8-1. Treatment and Associated Analytes

Treatment	Analyte
B/F/TAF	BIC
	FTC
	TAF

PK parameters to be estimated and analyzed in this substudy are listed and defined in PK abbreviations.

8.1. Estimation of Pharmacokinetic Parameters

Pharmacokinetic parameters will be estimated by application of a nonlinear model using standard noncompartmental methods (WinNonlin® software). The linear up/log down trapezoidal rule will be used in conjunction with the appropriate noncompartmental model (usually input Model 200 for oral dosing), with input values for dose, time of dose, plasma concentration, and corresponding real time values, based on drug dosing times whenever possible.

All predose sample times of less than time zero will be converted to zero. Samples below the limit of quantitation of the bioanalytical assays that occur prior to the achievement of the first quantifiable concentration will be assigned a concentration value of zero to prevent overestimation of the initial AUC. Samples that are BLQ at all other time points will be treated as missing data. The nominal time point for a key event or dosing interval (tau) may be used to permit direct calculation of AUC over specific time intervals. The appropriateness of this approach will be assessed by the pharmacokineticist on a profile-by-profile basis.

Accurate estimation of several PK parameters, such as λ_z and $t_{1/2}$, are dependent on the accurate estimation of the terminal elimination phase of the drug. The appropriateness of calculating these parameters will be evaluated upon inspection of PK data on a profile-by-profile basis by the pharmacokineticist.

8.2. Analysis for Intensive PK (PK Substudy Analysis Set)

Plasma concentration will be listed for all subjects and summarized by nominal time point for subjects in the PK substudy analysis set.

PK parameters estimated for each analyte will be listed for all subjects and summarized for subjects in the PK substudy analysis set.

The descriptive statistics (n, mean, SD, coefficient of variation [%CV], minimum, median, maximum, Q1, Q3, geometric mean, and its 95% CI) will be presented for plasma concentration and parameter data. For concentration values BLQ, the number of subjects with values of BLQ will be presented. For PK parameter data, the mean and SD of the natural-log transformed values will be presented in addition to the summaries mentioned above.

The following tables, figures and listings (TFLs) will be provided for the intensive PK analysis at Weeks 4 or 8 for each analyte for subjects in the PK substudy analysis set:

- Table with individual subject concentration and summary statistics at each time point for each analyte
- Table with individual subject PK parameters and summary statistics for each analyte
- Mean (SD) concentration vs. time figures – linear and semi-log plots for each analyte
- Median (Q1, Q3) concentration vs. time figures – linear and semi-log plots for each analyte
- Individual plasma concentration vs. time figures – linear and semi-log plots for each analyte
- Listing of the time points used in the calculation of the terminal elimination rate constant, λ_Z, for each analyte
- Listing of PK sampling details by subject including deviations in scheduled and actual draw times and procedures, individual blood sampling time deviations in minutes.
- Listing of study drug administration record for intensive PK dosing

8.3. Analysis for Trough and Postdose PK (PK Analysis Set)

Only PK plasma samples collected through October 20th, 2016 were analyzed and their concentration data are available in the Week 48 interim analysis. The following listings will be provided for trough and postdose PK analysis for subjects in the PK analysis set:

- Listing of PK sampling details (PK samples collected as “Predose” during intensive PK collection or “Trough” PK samples [defined as samples collected within a range of 20.0 to 28.0 hours, inclusive, after previous dosing time], will be marked in the listing).
- Listing of study drug administration record for PK dosing.

PK sampling details for the intensive PK, trough PK, and postdose PK samples will be included in one listing. Similarly, study drug administration records for the intensive PK, trough PK, and postdose PK samples will also be included in one listing.

8.4. Changes from Protocol-Specified Pharmacokinetic Analysis

No change from the protocol-specified PK analyses is planned.

9. SPECIAL POPULATION ANALYSES

9.1. Analyses for HIV/HBV Coinfected Subjects

Subjects with HIV/HBV coinfection at baseline are defined as subjects who meet any of the following two criteria:

- Positive HBsAg on or prior to the first dose date, 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.

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

- Positive HBsAg after the first dose date and on or prior to the date of permanent discontinuation of study drug, or
- Negative HBsAg, negative HBsAb, positive HBcAb, and quantifiable HBV DNA (ie, HBV DNA ≥ 20 IU/mL) after the first dose date and on or prior to the date of permanent discontinuation of study drug, or
- Experience any of the following adverse events (ie, selected MedDRA preferred terms from the SMQ of "Liver Infections") after the first dose date and on or prior to the date of permanent discontinuation of study drug: 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 study drug (if any):

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

9.2. Analyses for HIV/HCV Coinfected Subjects

Subjects with HIV/HCV coinfection at baseline 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. The following listings 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 are defined as subjects who are not HIV/HCV coinfected at baseline and meet any of the following criteria:

- Positive HCVAb after the first dose date and on or prior to the date of permanent discontinuation of study drug with baseline HCVAb Negative or missing, or

- Quantifiable HCV RNA (ie, HCV RNA ≥ 15 IU/mL) after the first dose date and on or prior to the date of permanent discontinuation of study drug, or

- Experience any of the following adverse events (ie, selected MedDRA PTs from the SMQ of "Liver Infections") after the first dose date and on or prior to the date of permanent discontinuation of study drug: 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 study drug:

- Listing of adverse events

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

10. REFERENCES

KDIGO Guideline Development Staff. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney international. Supplement 2013;3 (1):v-150.

LaVange LM, Koch GG. Randomization-Based Nonparametric (ANCOVA). In: D'Agostino Sr. RB, Sullivan LM, Massaro JM, eds. Wiley Encyclopedia of Clinical Trials. John Wiley & Sons, Inc.; 2008: 31-8. vol 4).

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. Revision 1. 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.

Phoenix WinNonlin® Version 6.4 (Certara USA, Inc., Princeton, NJ, USA.) is to be used for all PK analyses.

12. SAP REVISION

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

13. APPENDICES

Appendix 1. Study Procedures Tables
Appendix 2. Flowchart of US FDA-defined Snapshot Algorithm (for Switch Trial)
Appendix 3. Region Definition
Appendix 4. Selected Medical History
Appendix 5. Hepatic Events
Appendix 6. Programming Specification

Appendix 1. Study Procedures Tables

Appendix Table 1. Study Procedures Table (Blinded Phase)

Study Procedures	Screening[a]	Day 1[b]	End of Week[e,p]						Post-Week 48[e,q]	End of Blinded Treatment Visit	30-Day Follow-up[o]	Early Study Drugs DC[c]
			4	8	12	24	36	48	Every 12 Weeks			
Informed Consent	X											
Medical History	X											
Concomitant Medications	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[f]	X[f]
Complete/Symptom-Directed Physical Exam	**X**	**X**	X[d]	X[d]	X[d]	**X**	X[d]	**X**	X[d]	**X**	X[d,f]	**X**[f]
12-Lead ECG (performed supine)	X	X				X		X		X		X
Questionnaires		X	X		X			X				
DXA scan (spine & hip)[g]		X				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
Urinalysis	X	X	X	X	X	X	X	X	X	X	X[f]	X[f]
Urine Pregnancy Test[h]		X	X	X	X	X	X	X	X	X	X	X
Serum Pregnancy Test	X											
Chemistry Profile[i]	X	X	X	X	X	X	X	X	X	X	X[f]	X[f]
Metabolic Assessments[j]		X			X	X		X	X[r]	X		
Estimated Glomerular Filtration Rate	X	X	X	X	X	X	X	X	X	X	X[f]	X
Hematology Profile[k]	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
CD4+ Cell Count	X	X	X	X	X	X	X	X	X	X	X	X
Evaluations of inflammation and immune activation, platelet function and renal tubular function		X				X		X	X[r]	X		

Study Procedures	Screening[a]	Day 1[b]	End of Week[e,p]						Post-Week 48[e,q]	End of Blinded Treatment Visit	30-Day Follow-up[o]	Early Study Drugs DC[c]
			4	8	12	24	36	48	Every 12 Weeks			
Plasma & Urine Storage Sample		X	X	X	X	X	X	X	X	X		X
Whole Blood sample for potential HIV DNA genotyping		X										
HBV and HCV Serology	X							X	X[u]			
HIV-1 Genotype/Phenotype[e]												X[e]
Single PK Sample[l]				X		X	X					
Trough PK Samples[m]			X		X							
Optional PPD		X										
Randomization[t]		X										
Provide subject dosing diary to subjects		X	X	X	X	X						
Optional PK Substudy[n]			X	X								
Study Drug Dispensation		X[b]	X	X	X	X	X	X	X	X[s]		
Study Drug Accountability			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, with the exception of DXA.
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 Sections 6.13.1 and 6.13.2).
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 DXA scans to be performed in all eligible subjects on study drug, except for those in Germany, prior to or within 24 hours of the Day 1 Visit, Weeks 24, 48 (± 10 days), at End of Blinded Treatment Visit (± 10 days) and the ESDD visit (if the last scan was acquired > 12 weeks from the date of the End of Blinded Treatment Visit or ESDD Visit).
h Females of childbearing potential only. Positive urine pregnancy tests will be confirmed with a serum test.
i 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 × ULN) At Day 1, Weeks 12, 24, 48 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. Additionally: TSH will be analyzed at Screening, Day 1, Weeks 24 and 48 followed by every 24 weeks post Week 48, End of Blinded Treatment Visit, and Early Study Drugs Discontinuation visit.

j 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.
k CBC with differential and platelet count.
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.
n A PK substudy will be performed in a subset of subjects (n=30) at selected study sites. The pharmacokinetic substudy visit must occur at the **Week 4 or Week 8** visits. The substudy will include intensive PK profiling in plasma
o Only required for those subjects not enrolling in the OL 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.
p 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 36, unless otherwise specified. The visit window at Weeks 48 will be ± 6 weeks of the protocol-specified visit date.
q After Week 48, 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 48.
r To be performed every 24 weeks after Week 48 until End of Blinded Treatment Visit.
s Open label study drug, GS-9883/F/TAF FDC will be dispensed to subjects participating in the OL Rollover Extension for up to 96 weeks.
t 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.
u 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]								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		
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X	X	X[f]	X[f]
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		
DXA scan (spine & hip)[m]	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
Evaluations of inflammation and immune activation, platelet function and renal tubular function	X										
Plasma & Urine Storage Sample	X	X	X	X	X	X	X	X	X		X
HBV and HCV Serology					X				X		
HIV-1 Genotype/Phenotype[e]											X[e]

Study Procedures	End of Blinded Treatment Visit[a]	End of Week[e,l]								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		
Study Drug Dispensation[b]	X	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 48 visit and Gilead completes the Week 48 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, if safety and efficacy of GS-9883/F/TAF 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 GS-9883/F/TAF FDC in an OL extension phase for up to 96 weeks, or 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. Treatment assignments will be provided to the investigators within 30 days of the last subject completing the End of Blinded Treatment Visit.

b Open-label study drug, GS-9883/F/TAF FDC will be dispensed to subjects participating in the OL Rollover Extension for up to 96 weeks.

c Subjects who discontinue study drug during the OL 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 Sections 6.13.1 and 6.13.2).

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 × ULN). At the End of Blinded Treatment Visit, Week 24 OL and Week 48 OL, 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, Week 72 OL, Week 96 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). 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.

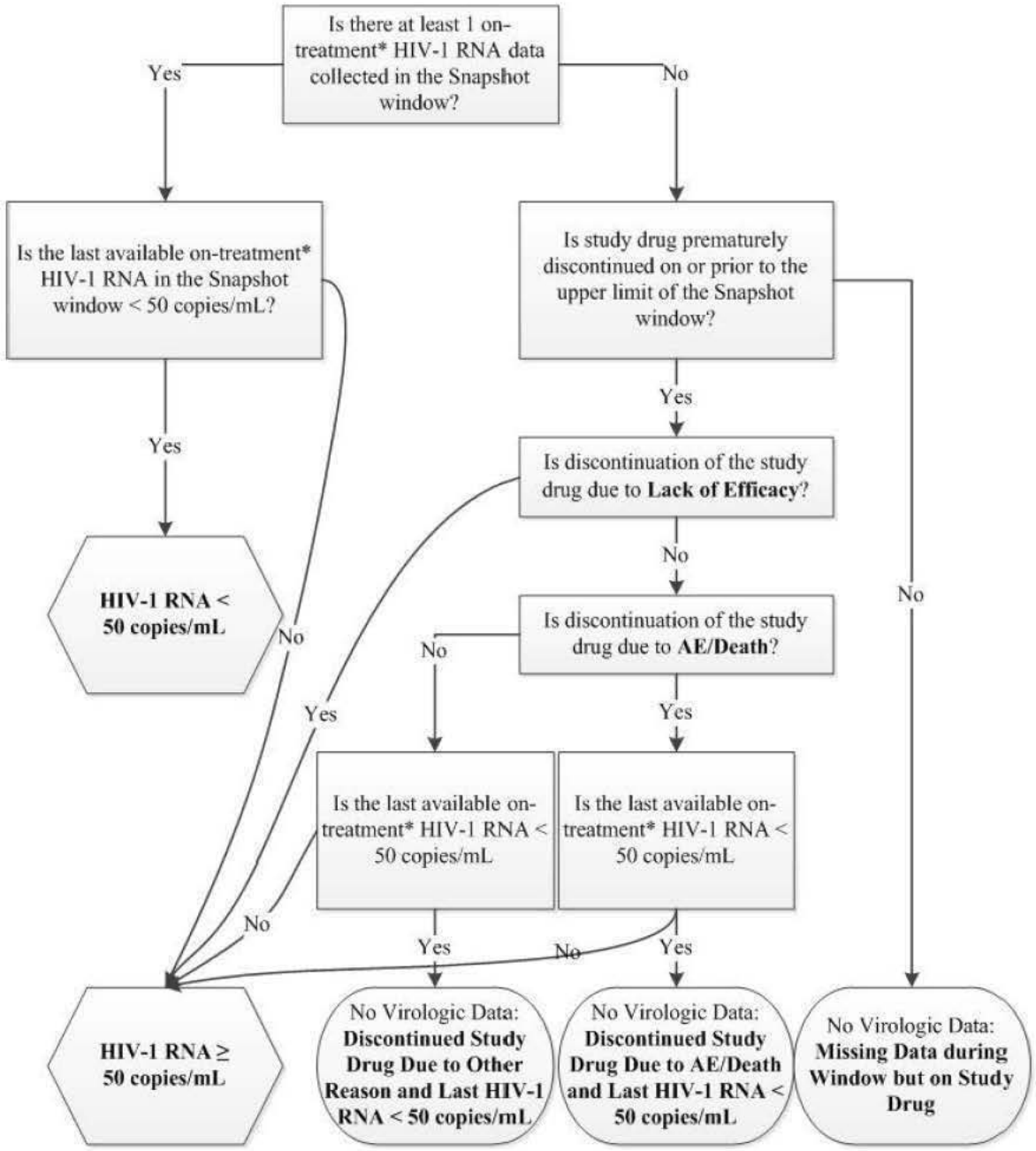
k Subjects who complete the OL Rollover Extension will be required to return to the clinic 30 days after the completion of study drugs for the 30-Day Follow-Up Visit. Subjects who permanently discontinue study drugs during the OL Rollover Extension will be asked to return to the clinic 30 days after 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 ± 6 days of the protocol-specified visit date based on the End of Blinded Treatment Visit date, unless otherwise specified.

m DXA scans to be performed in all eligible subjects on study drug, except for those in Germany, at the End of Blinded Treatment Visit (±10 days) if the last scan was acquired > 12 weeks from the date of the End of Blinded Treatment Visit.

Appendix 2. Flowchart of US FDA-defined Snapshot Algorithm (for Switch Trial)

The following flowchart for US FDA-defined snapshot algorithm is based on the US FDA Guidance on Human Immunodeficiency Virus-1 Infection: Developing Antiretroviral Drugs for treatment {U. S. Department of Health and Human Services 2015}.



* On-Treatment HIV-1 RNA data include all HIV-1 RNA data for subjects who are on-going and HIV-1 RNA data up to 1 day after the last dose date of study drug for subjects who prematurely discontinue or complete study drug.

Appendix 3. Region Definition

Region	Country Name	State	No. of Subjects in Safety Analysis Set or FAS (N=563)	Total No. of Subjects by Region in Safety Analysis Set or FAS Set (N=563)
Region 1	AUSTRALIA (AUS)		15	50
	CANADA (CAN)		35	
Region 2	BELGIUM (BEL)		2	112
	FRANCE (FRA)		12	
	GERMANY (DEU)		28	
	ITALY (ITA)		2	
	SPAIN (ESP)		62	
	UNITED KINGDOM (GBR)		6	
Region 3	United States (USA)	CA	82	103
	United States	HI	4	
	United States	WA	17	
Region 4	United States	AZ	5	63
	United States	NM	3	
	United States	TX	55	
Region 5	United States	IL	2	53
	United States	IN	2	
	United States	KY	6	
	United States	MI	18	
	United States	MN	14	
	United States	MO	10	
	United States	OH	1	
Region 6	United States	DC	35	64
	United States	MA	19	
	United States	NJ	2	
	United States	NY	7	
	United States	PA	1	
Region 7	United States	GA	21	39
	United States	LA	1	
	United States	NC	14	
	United States	SC	3	
Region 8	United States	FL	74	79
	United States	PR	5	

Note: A region is defined as multiple sites combined based on geographical locations. For example, for international studies, sites from each country or multiple neighboring counties were combined; and for US studies, sites from each state or multiple neighboring states were combined.

Appendix 4. Selected Medical History

Number and percentage of subjects with selected medical history of Diabetes Mellitus, Hypertension, Cardiovascular Disease, and Hyperlipidemia will be summarized by treatment as baseline disease characteristics. A subject who had medical history of one of these diseases is a subject who experience at least one of the following events:

- At least 1 medical history record with MedDRA PT (mh.MDRPT) in the selected PT listing for the corresponding disease with start date on or prior to the first dose date.
- At least 1 adverse event record with MedDRA PT (ae.MDRPT) in the selected PT listing for the corresponding disease with start date on or prior to the first dose date.
- At least 1 concomitant medications record with medication class and indication in the selected listing for the corresponding disease with start date on or prior to the first dose date.

If the start date is incomplete but the month and year (or year) of the start date is the same as or before the month and year (or year) of the first dosing date of study drug, then the event will be included. If the start date is completed missing, the event will be included.

Four variables (ie, DIABETES, HTENSION, CARDDIS, and HLIPDEM) will be added to raw Medical History and Adverse Events datasets. A medical history or an adverse event record will be flagged for a disease of interest if its MedDRA preferred term (PT) is included in the pre-specified PT list for the corresponding disease of interest, which include all PTs from the narrow or broad search of the following SMQs under MedDRA 19.1 provided by Gilead DSPH and reviewed by Gilead medical monitors.

Disease of Interest	SMQ Source
Diabetes Mellitus (DIABETES)	Hyperglycaemia/new onset diabetes mellitus (SMQ) – Narrow Scope Term
Hyperlipidemia (HLIPDEM)	Dyslipidaemia (SMQ)
Hypertension (HTENSION)	Hypertension (SMQ)
Cardiovascular disease (CARDDIS)	Ischaemic central nervous system vascular conditions (SMQ) - Narrow Scope Term
	Myocardial infarction (SMQ) - Narrow Scope Term
	Other ischaemic heart disease (SMQ) - Narrow Scope Term

Similarly, four variables (ie, DIABETES, HTENSION, CARDDIS, and HLIPDEM) will be added to raw Concomitant Medication dataset. A concomitant medication record will be flagged for a disease of interest if its medication class and indication included in the following listing for the corresponding disease of interest.

The selected combination of medication class and indication are listed as follows, which was reviewed by Gilead medical monitors.

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
Hypertension (HTENSION)			
1	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM		LISINOPRIL
2	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ANTI-HYPERTENSIVE	LOSARTAN
3	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ARTERIAL HYPENTENSION	RAMIPRIL
4	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ARTERIAL HYPERTENSION	CAPTOPRIL
5	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ARTERIAL HYPERTENSION	ENALAPRIL
6	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ARTERIAL HYPERTENSION	HYDROCHLOROTHIAZIDE W/OLMESARTAN
7	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ARTERIAL HYPERTENSION	OLMESARTAN MEDOXOMIL
8	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ARTERIAL HYPERTENSION	RAMIPRIL
9	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ARTERIAL HYPERTENSION	SALUTEC
10	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ARTERIAL HYPERTENSION	VALSARTAN
11	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ARTERIAL HYPERTENSION STAGE I	CAPTOPRIL
12	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ARTERIAL HYPERTENSION STAGE 1	CANDESARTAN
13	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	BENIGN ESSENTIAL HYPERTENSION	LISINOPRIL
14	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	BENIGN ESSENTIAL HYPERTENSION	LOSARTAN
15	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ESSENTIAL (PRIMARY)HYPERTESION	ZESTORETIC
16	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ESSENTIAL HYPERTENSION	COROVAL B
17	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ESSENTIAL HYPERTENSION	ENALAPRIL MALEATE
18	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ESSENTIAL HYPERTENSION	LISINOPRIL
19	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ESSENTIAL HYPERTENSION	LOSARTAN
20	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ESSENTIAL HYPERTENSION	TRIBENZOR

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
21	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ESSENTIAL HYPERTENSION	ZESTORETIC
22	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ESSENTIAL PRIMARY HYPERTENSION	IRBESARTAN
23	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HIGH BLOOD PRESSURE	COVERAM
24	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HIGH BLOOD PRESSURE	ENALAPRIL
25	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HIGH BLOOD PRESSURE	IRBESARTAN
26	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HIGH BLOOD PRESSURE	LISINOPRIL
27	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HIGH BLOOD PRESSURE	LOSARTAN
28	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HIGH BLOOD PRESSURE	LOSARTAN POTASSIUM
29	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HIGH BLOOD PRESSURE	RAMIPRIL
30	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HIGH BOLD PRESSURE	LOSARTAN
31	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HISTORY OF MYOCARDITIS	RAMIPRIL
32	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HTN	ZESTORETIC
33	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERRTENSION	ZESTORETIC
34	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTEENSION	LISINOPRIL
35	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	AMLODIPINE W/HYDROCHLOROTHIAZIDE/ VALSARTAN
36	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	AMLODIPINE W/VALSARTAN
37	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	BENAZEPRIL
38	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	BENAZEPRIL HYDROCHLORIDE
39	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	BENICAR HCT
40	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	BI PREDONIUM

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
41	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	CANDESARTAN
42	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	CANDESARTAN CILEXETIL
43	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	CAPTOPRIL
44	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	CO-DIOVAN
45	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	COROVAL B
46	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	DIOVAN AMLO
47	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	DIOVAN TRIPLE
48	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	EDARBYCLOR
49	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	ENALAPRIL
50	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	ENALAPRIL MALEATE
51	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	FOSINOPRIL
52	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	HYDROCHLOROTHIAZIDE W/LOSARTAN
53	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	HYZAAR
54	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	IRBESARTAN
55	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	KARVEA HCT
56	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	LISINOPRIL
57	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	LOSARTAN
58	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	LOSARTAN POTASSIUM
59	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	NAPRIX A
60	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	OLMESARTAN MEDOXOMIL
61	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	PERINDOPRIL ERBUMINE

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
62	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	PRITORPLUS
63	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	QUINAPRIL
64	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	RAMIPRIL
65	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	SALUTEC
66	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	TELMISARTAN
67	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	TRIBENZOR
68	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	VALSARTAN
69	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	VASERETIC
70	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION	ZESTORETIC
71	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION ESSENTIAL	CANDESARTAN CILEXETIL
72	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION ESSENTIAL	DIOVAN TRIPLE
73	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION, BENIGN	LISINOPRIL
74	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION, BILATERAL LOWER LEG SWELLING	LISINOPRIL
75	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION, ESSENTIAL	ZESTORETIC
76	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSION, WORSENING HYPERTENSION	LISINOPRIL
77	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSIONPROPHYLAXIS	RAMIPRIL
78	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSIVE	RAMIPRIL
79	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENSIVE CRISIS	CAPTOPRIL
80	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTENTION	LISINOPRIL
81	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTONIA	RAMIPRIL
82	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPOKALEMIA	LOSARTAN POTASSIUM

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
83	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	POOR CONTROL OF BLOOD PRESSURE	LISINOPRIL
84	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	PREVENTATIVE FOLLOWING ACUTE MYCARDIAL INFARCTION	PERINDOPRIL
85	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	PRIMARY ESSENTIAL HYPERTENSION	ENALAPRIL MALEATE
86	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	PROTEINURIA	BENAZEPRIL
87	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	PROTEINURIA	ENALAPRIL
88	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	PROTEINURIA	LISINOPRIL
89	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	WORSENING HYPERTENSION	BENAZEPRIL
90	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	WORSENING HYPERTENSION	PERINDOPRIL
91	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	WORSENING HYPERTENSION	PRETERAX ARGININE
92	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	WORSENING OF HYPERTENSION	LISINOPRIL
93	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	WORSENING OF HYPERTENSION	RAMIPRIL
94	ANTIHYPERTENSIVES	BENIGN HIGH BLOOD PRESSURE	DOXAZOSIN
95	ANTIHYPERTENSIVES	EXACERBATION OF HYPERTENSION	CLONIDINE
96	ANTIHYPERTENSIVES	HEADACHE	HYDRALAZINE
97	ANTIHYPERTENSIVES	HIGH BLOOD PRESSURE	CLONIDINE HYDROCHLORIDE
98	ANTIHYPERTENSIVES	HIGH BLOOD PRESSURE	RILMENIDINE
99	ANTIHYPERTENSIVES	HYPERTENSION	CLONIDINE
100	ANTIHYPERTENSIVES	HYPERTENSION	CLONIDINE HYDROCHLORIDE
101	ANTIHYPERTENSIVES	HYPERTENSION	DOXAZOSIN
102	ANTIHYPERTENSIVES	HYPERTENSION	DOXAZOSIN MESILATE
103	ANTIHYPERTENSIVES	HYPERTENSION	HYDRALAZINE
104	ANTIHYPERTENSIVES	HYPERTENSION	HYDRALAZINE HYDROCHLORIDE
105	ANTIHYPERTENSIVES	HYPERTENSION	METHYLDOPA
106	ANTIHYPERTENSIVES	HYPERTENSION	TADALAFIL

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
107	ANTIHYPERTENSIVES	PULMONARY HYPERTENSION	TADALAFIL
108	ANTIHYPERTENSIVES	VASODILATION-STENT PROCEDURE	HYDRALAZINE
109	ANTIHYPERTENSIVES	WORSENING HYPERTENSION	HYDRALAZINE HYDROCHLORIDE
110	BETA BLOCKING AGENTS	ARTERIAL HYPERTENSION	ATENOLOL
111	BETA BLOCKING AGENTS	ARTERIAL HYPERTENSION	METOPROLOL SUCCINATE
112	BETA BLOCKING AGENTS	ARTERIAL HYPERTENSION / ICHEMIC HEART DISEASE	BISOPROLOL
113	BETA BLOCKING AGENTS	ESSENTIAL HYPERTENSION	METOPROLOL
114	BETA BLOCKING AGENTS	HEART FAILURE AND HYPERTENSION	CARVEDILOL
115	BETA BLOCKING AGENTS	HEART HEALTH	ATENOLOL
116	BETA BLOCKING AGENTS	HIGH BLOOD PRESSURE	ATENOLOL
117	BETA BLOCKING AGENTS	HIGH BLOOD PRESSURE	BISOPROLOL W/HYDROCHLOROTHIAZIDE
118	BETA BLOCKING AGENTS	HIGH BLOOD PRESSURE	METOPROLOL
119	BETA BLOCKING AGENTS	HISTORY OF MYOCARDITIS	BISOPROLOL
120	BETA BLOCKING AGENTS	HYPERTENSION	ATENOLOL
121	BETA BLOCKING AGENTS	HYPERTENSION	BISOPROLOL FUMARATE
122	BETA BLOCKING AGENTS	HYPERTENSION	CARVEDILOL
123	BETA BLOCKING AGENTS	HYPERTENSION	LABETALOL
124	BETA BLOCKING AGENTS	HYPERTENSION	METOPROLOL
125	BETA BLOCKING AGENTS	HYPERTENSION	METOPROLOL SUCCINATE
126	BETA BLOCKING AGENTS	HYPERTENSION	METOPROLOL TARTRATE
127	BETA BLOCKING AGENTS	HYPERTENSION	NEBICARD V
128	BETA BLOCKING AGENTS	HYPERTENSION	NEBICARD-H
129	BETA BLOCKING AGENTS	HYPERTENSION	NEBIVOLOL
130	BETA BLOCKING AGENTS	HYPERTENSION	NEBIVOLOL HYDROCHLORIDE
131	BETA BLOCKING AGENTS	HYPERTENSION	PROPRANOLOL
132	BETA BLOCKING AGENTS	HYPERTENSION	PROPRANOLOL HYDROCHLORIDE
133	BETA BLOCKING AGENTS	HYPERTENSION AND MIGRAINE	ATENOLOL
134	BETA BLOCKING AGENTS	HYPERTENSION ESSENTIAL	ATENOLOL

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
135	BETA BLOCKING AGENTS	HYPERTENTION	METOPROLOL SUCCINATE
136	BETA BLOCKING AGENTS	HYPETENSION	BISOPROLOL
137	BETA BLOCKING AGENTS	PAROXYSM OF SINUS TACHYCARDIA	PROPRANOLOL
138	BETA BLOCKING AGENTS	PRIMARY ESSENTIAL HYPERTENSION	CARVEDILOL
139	BETA BLOCKING AGENTS	RAPID HEART BEAT	METOPROLOL SUCCINATE
140	CALCIUM CHANNEL BLOCKERS	ANTIHYPERTENSIVE	AMLODIPINE
141	CALCIUM CHANNEL BLOCKERS	ARTERIAL HYPERTENSION	AMLODIPINE
142	CALCIUM CHANNEL BLOCKERS	ARTERIAL HYPERTENSION	VERAPAMIL
143	CALCIUM CHANNEL BLOCKERS	ATRIAL FIBRILLATION	DILTIAZEM
144	CALCIUM CHANNEL BLOCKERS	ELEVATED BLOOD PRESSURE	AMLODIPINE
145	CALCIUM CHANNEL BLOCKERS	ELEVATED BLOOD PRESSURE	AMLODIPINE BESILATE
146	CALCIUM CHANNEL BLOCKERS	ESSENTIAL HYPERTENSION	AMLODIPINE
147	CALCIUM CHANNEL BLOCKERS	ESSENTIAL HYPERTENSION	AMLODIPINE BESILATE
148	CALCIUM CHANNEL BLOCKERS	ESSENTIAL HYPERTENSION	FELODIPINE
149	CALCIUM CHANNEL BLOCKERS	ESSENTIAL PRIMARY HYPERTENSION	AMLODIPINE
150	CALCIUM CHANNEL BLOCKERS	HIGH BLOOD PRESSURE	AMLODIPINE
151	CALCIUM CHANNEL BLOCKERS	HTN	AMLODIPINE
152	CALCIUM CHANNEL BLOCKERS	HYPERTENSION	AMLODIPINE
153	CALCIUM CHANNEL BLOCKERS	HYPERTENSION	AMLODIPINE BESILATE
154	CALCIUM CHANNEL BLOCKERS	HYPERTENSION	BARNIDIPINE HYDROCHLORIDE
155	CALCIUM CHANNEL BLOCKERS	HYPERTENSION	DILTIAZEM
156	CALCIUM CHANNEL BLOCKERS	HYPERTENSION	DILTIAZEM HYDROCHLORIDE
157	CALCIUM CHANNEL BLOCKERS	HYPERTENSION	FELODIPINE
158	CALCIUM CHANNEL BLOCKERS	HYPERTENSION	NIFEDIPINE
159	CALCIUM CHANNEL BLOCKERS	HYPERTENSION	VERAPAMIL
160	CALCIUM CHANNEL BLOCKERS	HYPERTENSION (ESSENTIAL/PRIMARY)	VERAPAMIL HYDROCHLORIDE
161	CALCIUM CHANNEL BLOCKERS	HYPERTENSION ESSENTIAL	FELODIPINE
162	CALCIUM CHANNEL BLOCKERS	HYPERTNESION	AMLODIPINE BESILATE
163	CALCIUM CHANNEL BLOCKERS	HYPTERTENSION	AMLODIPINE
164	CALCIUM CHANNEL BLOCKERS	PRESTUDY HYPERTENSION	AMLODIPINE

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
165	CALCIUM CHANNEL BLOCKERS	SECONDARY STROKE PREVENTION	AMLODIPINE
166	CALCIUM CHANNEL BLOCKERS	SICK SINUS SYNDROME	VERAPAMIL
167	CALCIUM CHANNEL BLOCKERS	WORSENING OF HYPERTENSION	AMLODIPINE
168	CARDIAC THERAPY	HYPERTENSION	UBIDECARENONE
169	DIURETICS	ARTERIAL HYPERTENSION	HYDROCHLOROTHIAZIDE
170	DIURETICS	BENIGN ESSENTIAL HYPERTENSION	HYDROCHLOROTHIAZIDE
171	DIURETICS	BORDERLINE HYPERTENSION	HYDROCHLOROTHIAZIDE
172	DIURETICS	DIURETIC	FUROSEMIDE
173	DIURETICS	ELEVATED BLOOD-PRESSURE READING, WITHOUT DIAGNOSIS OF HYPERTENSION	HYDROCHLOROTHIAZIDE
174	DIURETICS	ESSENTIAL HYPERTENSION	FUROSEMIDE
175	DIURETICS	ESSENTIAL HYPERTENSION	HYDROCHLOROTHIAZIDE
176	DIURETICS	HIGH BLOOD PRESSURE	HYDROCHLOROTHIAZIDE
177	DIURETICS	HYPERTENSION	AMILORIDE
178	DIURETICS	HYPERTENSION	BUMETANIDE
179	DIURETICS	HYPERTENSION	CHLORTALIDONE
180	DIURETICS	HYPERTENSION	DYAZIDE
181	DIURETICS	HYPERTENSION	FUROSEMIDE
182	DIURETICS	HYPERTENSION	HYDROCHLOROTHIAZIDE
183	DIURETICS	HYPERTENSION	INDAPAMIDE
184	DIURETICS	HYPERTENSION	MODURETIC
185	DIURETICS	HYPERTENSION	SPIRONOLACTONE
186	DIURETICS	HYPERTENSION	TRIAMTERENE
187	DIURETICS	HYPERTENSION, BENIGN	HYDROCHLOROTHIAZIDE
188	DIURETICS	HYPERTENTION	HYDROCHLOROTHIAZIDE
189	DIURETICS	WORSENING HYPERTENSION	HYDROCHLOROTHIAZIDE
190	LIPID MODIFYING AGENTS	HIGH BLOOD PRESSURE	PRAVASTATIN
191	LIPID MODIFYING AGENTS	HIGH BLOOD PRESSURE	PRAVASTATIN SODIUM

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
Diabetes Mellitus (DIABETES)			
1	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	DIABETES MELLITUS TYPE II	LISINOPRIL
2	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	TYPE 2 DIABETES	LISINOPRIL
3	ANTIHYPERTENSIVES	UNCONTROLLED DIABETES MELLITUS 2	CLONIDINE HYDROCHLORIDE
4	ANTIHYPERTENSIVES	UNCONTROLLED DIABETES MELLITUS 2	HYDRALAZINE HYDROCHLORIDE
5	BETA BLOCKING AGENTS	TYPE 2 DIABETES	METOPROLOL TARTRATE
6	DRUGS USED IN DIABETES	BORDERLINE DIABETES	METFORMIN
7	DRUGS USED IN DIABETES	DIABETES	DULAGLUTIDE
8	DRUGS USED IN DIABETES	DIABETES	GLIBENCLAMIDE
9	DRUGS USED IN DIABETES	DIABETES	GLICLAZIDE
10	DRUGS USED IN DIABETES	DIABETES	GLIMEPIRIDE
11	DRUGS USED IN DIABETES	DIABETES	GLIPIZIDE
12	DRUGS USED IN DIABETES	DIABETES	HUMAN MIXTARD
13	DRUGS USED IN DIABETES	DIABETES	INSULIN
14	DRUGS USED IN DIABETES	DIABETES	INSULIN ASPART
15	DRUGS USED IN DIABETES	DIABETES	INSULIN DETEMIR
16	DRUGS USED IN DIABETES	DIABETES	INSULIN GLARGINE
17	DRUGS USED IN DIABETES	DIABETES	INSULIN HUMAN
18	DRUGS USED IN DIABETES	DIABETES	INSULIN LISPRO
19	DRUGS USED IN DIABETES	DIABETES	METAGLIP
20	DRUGS USED IN DIABETES	DIABETES	METFORMIN
21	DRUGS USED IN DIABETES	DIABETES	METFORMIN HYDROCHLORIDE
22	DRUGS USED IN DIABETES	DIABETES	PIOGLITAZONE
23	DRUGS USED IN DIABETES	DIABETES	PIOGLITAZONE HYDROCHLORIDE
24	DRUGS USED IN DIABETES	DIABETES	SITAGLIPTIN
25	DRUGS USED IN DIABETES	DIABETES - TYPE I	INSULIN GLARGINE
26	DRUGS USED IN DIABETES	DIABETES - TYPE I	INSULIN LISPRO
27	DRUGS USED IN DIABETES	DIABETES 2	GLICLAZIDE
28	DRUGS USED IN DIABETES	DIABETES II	METFORMIN
29	DRUGS USED IN DIABETES	DIABETES KETOACIDOSIS	INSULIN

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
30	DRUGS USED IN DIABETES	DIABETES MELL. TYPE 2	INSULIN DETEMIR
31	DRUGS USED IN DIABETES	DIABETES MELL. TYPE 2	INSULIN LISPRO
32	DRUGS USED IN DIABETES	DIABETES MELL. TYPE 2	METFORMIN
33	DRUGS USED IN DIABETES	DIABETES MELLITIS TYPE 2	EMPAGLIFLOZIN
34	DRUGS USED IN DIABETES	DIABETES MELLITIS TYPE 2	GLIBENCLAMIDE
35	DRUGS USED IN DIABETES	DIABETES MELLITIS TYPE 2	INSULIN DETEMIR
36	DRUGS USED IN DIABETES	DIABETES MELLITIS TYPE 2	INSULIN LISPRO
37	DRUGS USED IN DIABETES	DIABETES MELLITUS	DULAGLUTIDE
38	DRUGS USED IN DIABETES	DIABETES MELLITUS	EXENATIDE
39	DRUGS USED IN DIABETES	DIABETES MELLITUS	GLIPIZIDE
40	DRUGS USED IN DIABETES	DIABETES MELLITUS	HUMAN MIXTARD
41	DRUGS USED IN DIABETES	DIABETES MELLITUS	INSULIN ASPART
42	DRUGS USED IN DIABETES	DIABETES MELLITUS	INSULIN DETEMIR
43	DRUGS USED IN DIABETES	DIABETES MELLITUS	INSULIN GLARGINE
44	DRUGS USED IN DIABETES	DIABETES MELLITUS	INSULIN HUMAN
45	DRUGS USED IN DIABETES	DIABETES MELLITUS	INSULIN LISPRO
46	DRUGS USED IN DIABETES	DIABETES MELLITUS	LIRAGLUTIDE
47	DRUGS USED IN DIABETES	DIABETES MELLITUS	METFORMIN
48	DRUGS USED IN DIABETES	DIABETES MELLITUS	METFORMIN HYDROCHLORIDE
49	DRUGS USED IN DIABETES	DIABETES MELLITUS	RISTFOR
50	DRUGS USED IN DIABETES	DIABETES MELLITUS	SITAGLIPTIN PHOSPHATE
51	DRUGS USED IN DIABETES	DIABETES MELLITUS TYP II	INSULIN LISPRO
52	DRUGS USED IN DIABETES	DIABETES MELLITUS TYP II	VELMETIA
53	DRUGS USED IN DIABETES	DIABETES MELLITUS 1	INSULIN GLARGINE
54	DRUGS USED IN DIABETES	DIABETES MELLITUS 1	INSULIN LISPRO
55	DRUGS USED IN DIABETES	DIABETES MELLITUS 11	GLIPIZIDE
56	DRUGS USED IN DIABETES	DIABETES MELLITUS 2	CANAGLIFLOZIN
57	DRUGS USED IN DIABETES	DIABETES MELLITUS 2	DULAGLUTIDE
58	DRUGS USED IN DIABETES	DIABETES MELLITUS 2	EXENATIDE
59	DRUGS USED IN DIABETES	DIABETES MELLITUS 2	GLIBOMET
60	DRUGS USED IN DIABETES	DIABETES MELLITUS 2	GLIMEPIRIDE
61	DRUGS USED IN DIABETES	DIABETES MELLITUS 2	GLIPIZIDE
62	DRUGS USED IN DIABETES	DIABETES MELLITUS 2	HUMAN MIXTARD

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
63	DRUGS USED IN DIABETES	DIABETES MELLITUS 2	INSULIN ASPART
64	DRUGS USED IN DIABETES	DIABETES MELLITUS 2	INSULIN DETEMIR
65	DRUGS USED IN DIABETES	DIABETES MELLITUS 2	INSULIN GLARGINE
66	DRUGS USED IN DIABETES	DIABETES MELLITUS 2	METFORMIN
67	DRUGS USED IN DIABETES	DIABETES MELLITUS 2	METFORMIN HYDROCHLORIDE
68	DRUGS USED IN DIABETES	DIABETES MELLITUS II	GLIPIZIDE
69	DRUGS USED IN DIABETES	DIABETES MELLITUS II	METFORMIN
70	DRUGS USED IN DIABETES	DIABETES MELLITUS II	SITAGLIPTIN
71	DRUGS USED IN DIABETES	DIABETES MELLITUS TYP 2	METFORMIN
72	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE 2	GLIPIZIDE
73	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE 2	INSULIN GLARGINE
74	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE 2	INSULIN LISPRO
75	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE 2	METFORMIN
76	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE 2	METFORMIN HYDROCHLORIDE
77	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE 2	SITAGLIPTIN PHOSPHATE
78	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	CANAGLIFLOZIN W/METFORMIN HYDROCHLORIDE
79	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	DULAGLUTIDE
80	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	GLIPIZIDE
81	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	HUMAN MIXTARD
82	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	INSULIN
83	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	INSULIN ASPART
84	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	INSULIN DETEMIR
85	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	INSULIN GLARGINE
86	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	INSULIN LISPRO
87	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	METFORMIN
88	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	METFORMIN HYDROCHLORIDE
89	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	NATEGLINIDE
90	DRUGS USED IN DIABETES	DIABETES MELLITUS TYPE II	SITAGLIPTIN PHOSPHATE
91	DRUGS USED IN DIABETES	DIABETES MELLITUS, TYPE II	METFORMIN HYDROCHLORIDE
92	DRUGS USED IN DIABETES	DIABETES TYPE 2	GLIPIZIDE

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
93	DRUGS USED IN DIABETES	DIABETES TYPE 2	HUMAN MIXTARD
94	DRUGS USED IN DIABETES	DIABETES TYPE 2	INSULIN ASPART
95	DRUGS USED IN DIABETES	DIABETES TYPE 2	INSULIN DETEMIR
96	DRUGS USED IN DIABETES	DIABETES TYPE 2	INSULIN GLARGINE
97	DRUGS USED IN DIABETES	DIABETES TYPE 2	INSULIN LISPRO
98	DRUGS USED IN DIABETES	DIABETES TYPE 2	KOMBIGLYZE
99	DRUGS USED IN DIABETES	DIABETES TYPE 2	METFORMIN
100	DRUGS USED IN DIABETES	DIABETES TYPE 2	SITAGLIPTIN PHOSPHATE
101	DRUGS USED IN DIABETES	DIABETES TYPE II	METFORMIN
102	DRUGS USED IN DIABETES	DIABETES, TYPE 2	GLIMEPIRIDE
103	DRUGS USED IN DIABETES	DIABETES, TYPE 2	LIRAGLUTIDE
104	DRUGS USED IN DIABETES	DIABETES, TYPE 2	PIOGLITAZONE
105	DRUGS USED IN DIABETES	DIABETIS	INSULIN GLARGINE
106	DRUGS USED IN DIABETES	DM2	GLIPIZIDE
107	DRUGS USED IN DIABETES	DM2	METFORMIN HYDROCHLORIDE
108	DRUGS USED IN DIABETES	HYPERGLICEMIA	GLIPIZIDE
109	DRUGS USED IN DIABETES	HYPERGLYCEMIA	INSULIN HUMAN
110	DRUGS USED IN DIABETES	HYPERGLYCEMIA	METFORMIN
111	DRUGS USED IN DIABETES	HYPERGLYCEMIA	METFORMIN HYDROCHLORIDE
112	DRUGS USED IN DIABETES	HYPERINSULINISM	METFORMIN
113	DRUGS USED IN DIABETES	HYPERTENSION	METFORMIN
114	DRUGS USED IN DIABETES	NONALCOHOLIC STEATOHEPATITIS	METFORMIN
115	DRUGS USED IN DIABETES	TYPE 1 DIABETES	INSULIN DEGLUDEC
116	DRUGS USED IN DIABETES	TYPE 1 DIABETES MELLITUS	INSULIN ASPART
117	DRUGS USED IN DIABETES	TYPE 1 DIABETES MELLITUS	INSULIN GLARGINE
118	DRUGS USED IN DIABETES	TYPE 2 DIABETES	GLICLAZIDE
119	DRUGS USED IN DIABETES	TYPE 2 DIABETES	HUMAN MIXTARD
120	DRUGS USED IN DIABETES	TYPE 2 DIABETES	INSULIN ASPART
121	DRUGS USED IN DIABETES	TYPE 2 DIABETES	INSULIN GLARGINE
122	DRUGS USED IN DIABETES	TYPE 2 DIABETES	INSULIN LISPRO
123	DRUGS USED IN DIABETES	TYPE 2 DIABETES	METFORMIN

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
124	DRUGS USED IN DIABETES	TYPE 2 DIABETES	METFORMIN HYDROCHLORIDE
125	DRUGS USED IN DIABETES	TYPE 2 DIABETES	SITAGLIPTIN PHOSPHATE
126	DRUGS USED IN DIABETES	TYPE 2 DIABETES MELLITUS	GLIMEPIRIDE
127	DRUGS USED IN DIABETES	TYPE 2 DIABETES MELLITUS	HUMAN MIXTARD
128	DRUGS USED IN DIABETES	TYPE 2 DIABETES MELLITUS	INSULIN HUMAN
129	DRUGS USED IN DIABETES	TYPE 2 DIABETES MELLITUS	LIRAGLUTIDE
130	DRUGS USED IN DIABETES	TYPE 2 DIABETES MELLITUS	METFORMIN HYDROCHLORIDE
131	DRUGS USED IN DIABETES	TYPE 2 DIABETES MELLITUS	PIOGLITAZONE
132	DRUGS USED IN DIABETES	TYPE II DIABETES	CANAGLIFLOZIN W/METFORMIN HYDROCHLORIDE
133	DRUGS USED IN DIABETES	TYPE II DIABETES	DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE W/METFO
134	DRUGS USED IN DIABETES	TYPE II DIABETES	GLIPIZIDE
135	DRUGS USED IN DIABETES	TYPE II DIABETES	INSULIN
136	DRUGS USED IN DIABETES	TYPE II DIABETES	INSULIN DETEMIR
137	DRUGS USED IN DIABETES	TYPE II DIABETES	INSULIN GLARGINE
138	DRUGS USED IN DIABETES	TYPE II DIABETES	LIRAGLUTIDE
139	DRUGS USED IN DIABETES	TYPE II DIABETES	METFORMIN
140	DRUGS USED IN DIABETES	TYPE II DIABETES	SITAGLIPTIN PHOSPHATE
141	DRUGS USED IN DIABETES	TYPE II DIABETES MELLITUS	EXENATIDE
142	DRUGS USED IN DIABETES	TYPE II DIABETES MELLITUS	METFORMIN
143	DRUGS USED IN DIABETES	TYPE II DIABETES MELLITUS	METFORMIN HYDROCHLORIDE
144	DRUGS USED IN DIABETES	UNCONTROLLED DIABETES MELLITUS 2	INSULIN LISPRO
145	DRUGS USED IN DIABETES	UNCONTROLLED DIABETES MELLITUS WITH HYPERGLICEMIA	GLIPIZIDE
146	DRUGS USED IN DIABETES	UNCONTROLLED DIABETES MELLITUS WITH HYPERGLICEMIA	HUMAN MIXTARD
147	DRUGS USED IN DIABETES	UNCONTROLLED DM2	INSULIN DETEMIR
148	UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	HERBAL SUPPLEMENT	GLYCINE MAX EXTRACT
149	LIPID MODIFYING AGENTS	DIABETES MELLITUS TYPE II	PRAVASTATIN

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
Cardiovascular (CARDDIS)			
1	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	ACUTE MYOCARDIAL INFARCTION	IRBESARTAN
2	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	CARDIOMYOPATHY	LISINOPRIL
3	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	CARDIOMYOPATHY	RAMIPRIL
4	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	CONGESTIVE HEART FAILURE	LISINOPRIL
5	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	CORONARY ARTERY DISEASE	RAMIPRIL
6	BETA BLOCKING AGENTS	ACUTE MYOCARDIAL INFARCTION	BISOPROLOL FUMARATE
7	BETA BLOCKING AGENTS	ANTI-ARRHYTHMIC	SOTALOL
8	BETA BLOCKING AGENTS	ATHEROSCLEROTIC HEART DISEASE OF NATIVE CORONARY ARTERY WITHOUT ANGINA PECTORIS	CARVEDILOL
9	BETA BLOCKING AGENTS	ATRIAL FIBRILATION	ATENOLOL
10	BETA BLOCKING AGENTS	ATRIAL FIBRILATION	METOPROLOL
11	BETA BLOCKING AGENTS	ATRIAL FIBRILLATION	METOPROLOL
12	BETA BLOCKING AGENTS	ATRIAL FIBRILLATION	METOPROLOL TARTRATE
13	BETA BLOCKING AGENTS	ATYPICAL CHEST PAIN	LABETALOL
14	BETA BLOCKING AGENTS	BRUGADA SYNDROME	BISOPROLOL
15	BETA BLOCKING AGENTS	CAD	METOPROLOL SUCCINATE
16	BETA BLOCKING AGENTS	CADRIOMYOPATHY	BISOPROLOL
17	BETA BLOCKING AGENTS	CARDIAC PACEMAKER INSITU	METOPROLOL
18	BETA BLOCKING AGENTS	CARDIAC PROPHYLAXIS	CARVEDILOL
19	BETA BLOCKING AGENTS	CARDIOMYOPATHY	CARVEDILOL
20	BETA BLOCKING AGENTS	CHEST TIGHTNESS	BISOPROLOL
21	BETA BLOCKING AGENTS	CONGESTIVE HEART FAILURE	ATENOLOL
22	BETA BLOCKING AGENTS	CONGESTIVE HEART FAILURE	CARVEDILOL
23	BETA BLOCKING AGENTS	CONTROLLED HYPERTENSION	TENORETIC
24	BETA BLOCKING AGENTS	CORONARY ARTERY DISEASE	METOPROLOL
25	BETA BLOCKING AGENTS	CORONARY ARTERY DISEASE	METOPROLOL SUCCINATE

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
26	BETA BLOCKING AGENTS	CORONARY ARTERY STENOSIS	METOPROLOL
27	BETA BLOCKING AGENTS	DYSRHYTHMIA	BISOPROLOL FUMARATE
28	BETA BLOCKING AGENTS	HEART FAILURE AND HYPERTENSION	CARVEDILOL
29	BETA BLOCKING AGENTS	INTERMITTENT ARRHYTHMIA	BISOPROLOL
30	BETA BLOCKING AGENTS	MITRAL INSUFFICIENCY	BISOPROLOL
31	BETA BLOCKING AGENTS	PREVENTATIVE FOLLOWING ACUTE MYCARDIAL INFARCTION	BISOPROLOL
32	BETA BLOCKING AGENTS	SICK SINUS SYNDROME	METOPROLOL
33	BETA BLOCKING AGENTS	SUPRA VENTRICULAR TACHYCARDIA	ATENOLOL
34	BETA BLOCKING AGENTS	SUPRAVENTRICULAR TACHYCARDIA	ATENOLOL
35	BETA BLOCKING AGENTS	SUPRAVENTRICULAR TACHYCARDIA	METOPROLOL
36	BETA BLOCKING AGENTS	TACHYCARDIA	ATENOLOL
37	CALCIUM CHANNEL BLOCKERS	CORONARY ARTERY DISEASE	AMLODIPINE
38	CALCIUM CHANNEL BLOCKERS	CORONARY ARTERY DISEASE	AMLODIPINE BESILATE
39	CALCIUM CHANNEL BLOCKERS	SUPRAVENTRICULAR TACHYCARDIA	VERAPAMIL
40	CARDIAC THERAPY	ACUTE MYOCARDIAL INFARCTION	AMIODARONE HYDROCHLORIDE
41	CARDIAC THERAPY	ACUTE MYOCARDIAL INFARCTION	ISOSORBIDE DINITRATE
42	CARDIAC THERAPY	ALLERGIC REACTION	EPINEPHRINE
43	CARDIAC THERAPY	ANGINA	GLYCERYL TRINITRATE
44	CARDIAC THERAPY	ANGINA PECTORIS	RANOLAZINE
45	CARDIAC THERAPY	ANGIOGRAM/STENT	ADENOSINE
46	CARDIAC THERAPY	ANGIONEUROTIC EDEMA	EPINEPHRINE
47	CARDIAC THERAPY	ANTIARRHYTHMIC AGENT	FLECAINIDE ACETATE
48	CARDIAC THERAPY	ATRIAL FIBRILLATION	DIGOXIN
49	CARDIAC THERAPY	ATRIAL FIBRILLATION	FLECAINIDE ACETATE
50	CARDIAC THERAPY	ATYPICAL CHEST PAIN	GLYCERYL TRINITRATE
51	CARDIAC THERAPY	CAD	UBIDECARENONE
52	CARDIAC THERAPY	CARDIOMYOPATHY	ISOSORBIDE DINITRATE

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
53	CARDIAC THERAPY	CARDIOVASCULAR DISEASE PROPHYLAXIS	UBIDECARENONE
54	CARDIAC THERAPY	CHEST PAIN	GLYCERYL TRINITRATE
55	CARDIAC THERAPY	CHEST PAINS	GLYCERYL TRINITRATE
56	CARDIAC THERAPY	CHESTPAIN	GLYCERYL TRINITRATE
57	CARDIAC THERAPY	CORONARY ARTERY DISEASE	GLYCERYL TRINITRATE
58	CARDIAC THERAPY	CORONARY ARTERY DISEASE	ISOSORBIDE MONONITRATE
59	CARDIAC THERAPY	HYPERLIPIDEMIA	ISOSORBIDE MONONITRATE
60	CARDIAC THERAPY	NSTEMI	ISOSORBIDE DINITRATE
61	CARDIAC THERAPY	PERIOP STRESS TEST	REGADENOSON
62	CARDIAC THERAPY	PROPHYLAXIS	GLYCERYL TRINITRATE
63	CARDIAC THERAPY	PROPHYLAXIS FOR CARDIAC HEALTH	UBIDECARENONE
64	CARDIAC THERAPY	SUPRAVENTRICULAR TACHYCARDIA	ADENOSINE
65	CARDIAC THERAPY	UNCONTROLLED DIABETES MELLITUS 2	AMIODARONE HYDROCHLORIDE
66	CARDIAC THERAPY	UNCONTROLLED DIABETES MELLITUS 2	GLYCERYL TRINITRATE
67	DIURETICS	ACUTE RESPIRATORY FAILURE	FUROSEMIDE
68	DIURETICS	AORTIC VALVE REPLACEMENT	FUROSEMIDE
69	DIURETICS	CHF	BUMETANIDE
70	DIURETICS	CHF	HYDROCHLOROTHIAZIDE
71	DIURETICS	CHF	METOLAZONE
72	DIURETICS	CONGESTIVE HEART FAILURE	BUMETANIDE
73	DIURETICS	CONGESTIVE HEART FAILURE	FUROSEMIDE
74	DIURETICS	CONGESTIVE HEART FAILURE	HYDROCHLOROTHIAZIDE
75	DIURETICS	CONGESTIVE HEART FAILURE	METOLAZONE
76	DIURETICS	CONGESTIVE HEART FAILURE	SPIRONOLACTONE
77	DIURETICS	CORONARY ARTERY DISEASE	HYDROCHLOROTHIAZIDE
78	DIURETICS	CORONARY ARTERY DISEASE	FUROSEMIDE

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
79	DIURETICS	ELEVATION OF BLOOD PRESSURE	FUROSEMIDE
80	DIURETICS	MITRAL INSUFFICIENCY	TORASEMIDE
81	DIURETICS	TRANSGENGER	SPIRONOLACTONE
82	LIPID MODIFYING AGENTS	ACUTE MYOCARDIAL INFARCTION	ATORVASTATIN CALCIUM
83	LIPID MODIFYING AGENTS	ACUTE MYOCARDIAL INFARCTION	OMEGA-3 TRIGLYCERIDES
84	LIPID MODIFYING AGENTS	ATHEROSCLEROTIC HEART DISEASE OF NATIVE CORONARY ARTERY WITHOUT ANGINA PECTORIS	SIMVASTATIN
85	LIPID MODIFYING AGENTS	BASILAR ARTERY THROMBUS	ATORVASTATIN CALCIUM
86	LIPID MODIFYING AGENTS	CAD	PRAVASTATIN SODIUM
87	LIPID MODIFYING AGENTS	CAD	ROSUVASTATIN CALCIUM
88	LIPID MODIFYING AGENTS	CARDIAC PROPHYLAXIS	ATORVASTATIN
89	LIPID MODIFYING AGENTS	CARDIAC PROPHYLAXIS	FISH OIL
90	LIPID MODIFYING AGENTS	CARDIOVASCULAR PROPHYLAXIS	ATORVASTATIN CALCIUM
91	LIPID MODIFYING AGENTS	CHEST TIGHTNESS	ATORVASTATIN
Hyperlipidemia (HLIPDEM)			
1	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	HYPERTRIGLYCERIDEMIA	LISINOPRIL
2	ANTIHYPERTENSIVES	HYPERCHOLESTEROLEMIA	DOXAZOSIN MESILATE
3	CARDIAC THERAPY	HYPERCHOLESTEROLEMIA	UBIDECARENONE
4	LIPID MODIFYING AGENTS	ABNORMAL LIPIDS	ATORVASTATIN
5	LIPID MODIFYING AGENTS	CARDIAC PROPHYLAXIS	ROSUVASTATIN
6	LIPID MODIFYING AGENTS	CHOLESTEROL	ROSUVASTATIN
7	LIPID MODIFYING AGENTS	CHOLESTEROL	ROSUVASTATIN CALCIUM
8	LIPID MODIFYING AGENTS	CHOLESTEROLEAMIA	ATORVASTATIN
9	LIPID MODIFYING AGENTS	CHOLESTERORL	ROSUVASTATIN CALCIUM
10	LIPID MODIFYING AGENTS	CORONARY ARTERY DISEASE	ATORVASTATIN
11	LIPID MODIFYING AGENTS	CORONARY ARTERY DISEASE	EZETIMIBE
12	LIPID MODIFYING AGENTS	CORONARY ARTERY DISEASE	FENOFIBRATE
13	LIPID MODIFYING AGENTS	CORONARY ARTERY DISEASE	ROSUVASTATIN CALCIUM
14	LIPID MODIFYING AGENTS	CORONARY ARTERY DISEASE PROPHYLAXIS	ATORVASTATIN

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
15	LIPID MODIFYING AGENTS	DIET SUPPLEMENT	FISH OIL
16	LIPID MODIFYING AGENTS	DIETARY SUPPLEMENT	FISH OIL
17	LIPID MODIFYING AGENTS	DIETARY SUPPLEMENTS	FISH OIL
18	LIPID MODIFYING AGENTS	DYSLIPEDEMIA	ROSUVASTATIN CALCIUM
19	LIPID MODIFYING AGENTS	DYSLIPIDAEMIA	ATORVASTATIN
20	LIPID MODIFYING AGENTS	DYSLIPIDEMIA	ATORVASTATIN
21	LIPID MODIFYING AGENTS	DYSLIPIDEMIA	FENOFIBRATE
22	LIPID MODIFYING AGENTS	DYSLIPIDEMIA	FISH OIL
23	LIPID MODIFYING AGENTS	DYSLIPIDEMIA	GEMFIBROZIL
24	LIPID MODIFYING AGENTS	DYSLIPIDEMIA	PRAVASTATIN
25	LIPID MODIFYING AGENTS	DYSLIPIDEMIA	ROSUVASTATIN
26	LIPID MODIFYING AGENTS	DYSLIPIDEMIA, WORSENING	ROSUVASTATIN
27	LIPID MODIFYING AGENTS	DYSLIPIDERMIA	PRAVASTATIN
28	LIPID MODIFYING AGENTS	ELEVATED CHOLESTEROL	SIMVASTATIN
29	LIPID MODIFYING AGENTS	ELEVATED LIPIDS	ATORVASTATIN
30	LIPID MODIFYING AGENTS	ELEVATED LIPIDS	ATORVASTATIN CALCIUM
31	LIPID MODIFYING AGENTS	ELEVATED TRIGLYCERIDES	FISH OIL
32	LIPID MODIFYING AGENTS	HIGH CHOLESTEROL	ATORVASTATIN
33	LIPID MODIFYING AGENTS	HIGH CHOLESTEROL	ATORVASTATIN CALCIUM
34	LIPID MODIFYING AGENTS	HIGH CHOLESTEROL	GEMFIBROZIL
35	LIPID MODIFYING AGENTS	HIGH CHOLESTEROL	LOVASTATIN
36	LIPID MODIFYING AGENTS	HIGH CHOLESTEROL	PRAVASTATIN
37	LIPID MODIFYING AGENTS	HIGH CHOLESTEROL	ROSUVASTATIN CALCIUM
38	LIPID MODIFYING AGENTS	HIGH CHOLESTEROL	SIMVASTATIN
39	LIPID MODIFYING AGENTS	HIGH CHOLESTROL	ATORVASTATIN
40	LIPID MODIFYING AGENTS	HIGH PLASMA LIPIDS	ATORVASTATIN
41	LIPID MODIFYING AGENTS	HIGH TRIGLYCERIDES	FENOFIBRATE
42	LIPID MODIFYING AGENTS	HIGH TRIGLYCERIDES AND HYPERCHOLESTEROLEMIA	ATORVASTATIN
43	LIPID MODIFYING AGENTS	HIPERCOLESTEROLEMIA	ATORVASTATIN
44	LIPID MODIFYING AGENTS	HIPERCOLESTEROLEMIA	ATORVASTATIN CALCIUM
45	LIPID MODIFYING AGENTS	HIPERCOLESTEROLEMIA	SIMVASTATIN
46	LIPID MODIFYING AGENTS	HYERLIPIDEMIA	OMEGA-3-ACID ETHYL ESTER
47	LIPID MODIFYING AGENTS	HYPERCHOLESTERIMIA	FENOFIBRATE

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
48	LIPID MODIFYING AGENTS	HYPERCHOLESTERINAEMIA	ATORVASTATIN
49	LIPID MODIFYING AGENTS	HYPERCHOLESTERINAEMIA	PRAVASTATIN
50	LIPID MODIFYING AGENTS	HYPERCHOLESTERINEMIA	PRAVASTATIN
51	LIPID MODIFYING AGENTS	HYPERCHOLESTERINEMIA	SIMVASTATIN
52	LIPID MODIFYING AGENTS	HYPERCHOLESTEROL	PRAVASTATIN
53	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLAEMIA	ATORVASTATIN
54	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLAEMIA	PRAVASTATIN
55	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLAEMIA	ROSUVASTATIN
56	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLAEMIA	SIMVASTATIN
57	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	ATORVASTATIN
58	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	ATORVASTATIN CALCIUM
59	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	EZETIMIBE
60	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	FENOFIBRATE
61	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	FISH OIL
62	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	LOVASTATIN
63	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	PITAVASTATIN CALCIUM
64	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	PRAVASTATIN
65	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	PRAVASTATIN SODIUM
66	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	ROSUVASTATIN
67	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	ROSUVASTATIN CALCIUM
68	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	SIMVASTATIN
69	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA (PURE) AND MIXED HYPERLIPIDEMIA	ROSUVASTATIN CALCIUM
70	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLMIA	PRAVASTATIN SODIUM
71	LIPID MODIFYING AGENTS	HYPERCHOLESTROLEMIA	ATORVASTATIN
72	LIPID MODIFYING AGENTS	HYPERCHOLESTROLEMIA	ATORVASTATIN CALCIUM
73	LIPID MODIFYING AGENTS	HYPERCHOLESTROLEMIA	FENOFIBRATE
74	LIPID MODIFYING AGENTS	HYPERCHOLSTEROAEMIA	ATORVASTATIN CALCIUM
75	LIPID MODIFYING AGENTS	HYPERCOLESTEROLEMIA	SIMVASTATIN
76	LIPID MODIFYING AGENTS	HYPERLIDEMIA	ROSUVASTATIN CALCIUM
77	LIPID MODIFYING AGENTS	HYPERLIDIPEMIA	ATORVASTATIN
78	LIPID MODIFYING AGENTS	HYPERLIPDEMIA	ROSUVASTATIN CALCIUM
79	LIPID MODIFYING AGENTS	HYPERLIPEDMIA-MIXED	ATORVASTATIN
80	LIPID MODIFYING AGENTS	HYPERLIPIDAEMIA	ATORVASTATIN

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
81	LIPID MODIFYING AGENTS	HYPERLIPIDAEMIA	FENOFIBRATE
82	LIPID MODIFYING AGENTS	HYPERLIPIDAEMIA	PRAVASTATIN
83	LIPID MODIFYING AGENTS	HYPERLIPIDAEMIA	PRAVASTATIN SODIUM
84	LIPID MODIFYING AGENTS	HYPERLIPIDAEMIA	ROSUVASTATIN
85	LIPID MODIFYING AGENTS	HYPERLIPIDAEMIA	ROSUVASTATIN CALCIUM
86	LIPID MODIFYING AGENTS	HYPERLIPIDEMA	ATORVASTATIN
87	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	ATORVASTATIN
88	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	ATORVASTATIN CALCIUM
89	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	COLESEVELAM HYDROCHLORIDE
90	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	EICOSAPENTAENOIC ACID ETHYL ESTER
91	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	EZETIMIBE
92	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	FENOFIBRATE
93	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	FENOFIBRIC ACID
94	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	FISH OIL
95	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	GEMFIBROZIL
96	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	LOVASTATIN
97	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	OMEGA-3-ACID ETHYL ESTER
98	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	PELAGO
99	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	PRAVASTATIN
100	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	PRAVASTATIN SODIUM
101	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	ROSUVASTATIN
102	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	ROSUVASTATIN CALCIUM
103	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	SIMVASTATIN
104	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA PREVENTION	ROSUVASTATIN CALCIUM
105	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA,	PRAVASTATIN
106	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA, MIXED	ATORVASTATIN CALCIUM
107	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA, MIXED	FENOFIBRATE
108	LIPID MODIFYING AGENTS	HYPERTENSION	ATORVASTATIN
109	LIPID MODIFYING AGENTS	HYPERTENSION	PRAVASTATIN
110	LIPID MODIFYING AGENTS	HYPERTRIGLYCERDEMIA	ATORVASTATIN
111	LIPID MODIFYING AGENTS	HYPERTRIGLYCERIDEMIA	ATORVASTATIN CALCIUM
112	LIPID MODIFYING AGENTS	HYPERTRIGLYCERIDEMIA	FENOFIBRATE

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
113	LIPID MODIFYING AGENTS	HYPERTRIGLYCERIDEMIA	FENOFIBRIC ACID
114	LIPID MODIFYING AGENTS	HYPERTRIGLYCERIDEMIA	FIBRATES
115	LIPID MODIFYING AGENTS	HYPERTRIGLYCERIDEMIA	FISH OIL
116	LIPID MODIFYING AGENTS	HYPERTRIGLYCERIDEMIA	OMEGA-3 TRIGLYCERIDES
117	LIPID MODIFYING AGENTS	HYPERTRIGLYCERIDEMIA	PRAVASTATIN
118	LIPID MODIFYING AGENTS	HYPERTRIGLYCERIDEMIA,HYPERCHOLESTEROLEMIA	ATORVASTATIN
119	LIPID MODIFYING AGENTS	HYPERTRIGLYERIDEMIA	GEMFIBROZIL
120	LIPID MODIFYING AGENTS	HYPERTRYGLYCERIDEMIA	PRAVASTATIN
121	LIPID MODIFYING AGENTS	INDICATION HYPERLIPIDEMIA	FENOFIBRATE
122	LIPID MODIFYING AGENTS	IRRITABLE BOWEL SYNDROME	FISH OIL
123	LIPID MODIFYING AGENTS	ISCHEMIC HEART DISEASE	ROSUVASTATIN CALCIUM
124	LIPID MODIFYING AGENTS	LDL-CHOLESTEROL GRADE 3 ELEVATION	ROSUVASTATIN
125	LIPID MODIFYING AGENTS	MIXED DYSLIPIDEMIA	FENOFIBRATE
126	LIPID MODIFYING AGENTS	MIXED DYSLIPIDEMIA	ROSUVASTATIN CALCIUM
127	LIPID MODIFYING AGENTS	MIXED HYPERLIPDEMIA	ATORVASTATIN
128	LIPID MODIFYING AGENTS	MIXED HYPERLIPIDEMIA	ATORVASTATIN
129	LIPID MODIFYING AGENTS	MIXED HYPERLIPIDEMIA	FENOFIBRATE
130	LIPID MODIFYING AGENTS	MIXED HYPERLIPIDEMIA	GEMFIBROZIL
131	LIPID MODIFYING AGENTS	NUTRITION SUPPLEMENT	FISH OIL
132	LIPID MODIFYING AGENTS	NUTRITIONAL SUPPLEMENT	FISH OIL
133	LIPID MODIFYING AGENTS	NUTRITIONAL SUPPLEMENT	OMEGA-3 FATTY ACIDS
134	LIPID MODIFYING AGENTS	PREVENTATIVE FOLLOWING ACUTE MYCARDIAL INFARCTION	ATORVASTATIN
135	LIPID MODIFYING AGENTS	PREVENTION FOR HYPERCHOLESTEROLEMIA	OMEGA-3 FATTY ACIDS
136	LIPID MODIFYING AGENTS	PREVENTIVE	FISH OIL W/LINUM USITATISSIMUM SEED OIL
137	LIPID MODIFYING AGENTS	PROPHYLAXIS	FISH OIL
138	LIPID MODIFYING AGENTS	PURE HYPERCHOLESTEROLEMIA	ATORVASTATIN
139	LIPID MODIFYING AGENTS	SECONDARY STROKE PREVENTION	ATORVASTATIN
140	LIPID MODIFYING AGENTS	STROKE PROPHYLAXIS	ATORVASTATIN

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
141	LIPID MODIFYING AGENTS	SUPPLEMENT	FISH OIL
142	LIPID MODIFYING AGENTS	SUPPLEMENT	OMEGA 3 6 9
143	LIPID MODIFYING AGENTS	SUPPLEMENT	OMEGA-3 FATTY ACIDS
144	LIPID MODIFYING AGENTS	SUPPLEMENT	OMEGA-3 FATTY ACIDS W/OMEGA-6 FATTY ACIDS
145	LIPID MODIFYING AGENTS	SUPPLEMENT	OMEGA-3-ACID ETHYL ESTER
146	LIPID MODIFYING AGENTS	SUPPLEMENT/ HYPERLIPIDEMIA	FISH OIL
147	LIPID MODIFYING AGENTS	SUPPLEMENTAL USE	FISH OIL
148	LIPID MODIFYING AGENTS	SUPPLEMETN	FISH OIL
149	LIPID MODIFYING AGENTS	UNCONTROLLED DIABETES MELLITUS 2	ATORVASTATIN
150	LIPID MODIFYING AGENTS	WORSENING HYPERLIPIDEMIA	ATORVASTATIN
151	LIPID MODIFYING AGENTS	WORSENING OF HYPERLIPIDEMIA	FISH OIL
152	LIPID MODIFYING AGENTS	HIGH CHOLESTEROL	NICOTINIC ACID
153	LIPID MODIFYING AGENTS	HYPERCHOLESTEROLEMIA	NICOTINIC ACID
154	LIPID MODIFYING AGENTS	HYPERLIPIDEMIA	NICOTINIC ACID
155	LIPID MODIFYING AGENTS	MIXED HYPERLIPIDEMIA	NICOTINIC ACID

Appendix 5. Hepatic Events

An adverse event record will be flagged as a hepatic event if its MedDRA PT is included in this pre-specified PT list, which includes all PTs from the broad search of the following 15 SMQs under MedDRA 19.1 provided by Gilead DSPH 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 6. Programming Specification

1) AGE calculated as follows:

   a) AGE (years) is calculated from the number of days between the date of birth (DOB) and Day 1 (first dose date),

   b) 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),

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

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

   e) 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.

   Age for laboratory test reference range will be based on the age at the sample collection date.

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 were 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 non-missing RGMNDTN in the IXRSRAND dataset), and confirmed by the eCRF ENROLL dataset (ie, ENROLLYN = "Yes" in ENROLL dataset).

5) 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.

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

7) 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.

8) SAS codes for the treatment comparison for demographics and baseline characteristics tables.

   a) CMH test for nominal variable (Y), the p-value from general association test should be used for nominal variable:

```
proc freq order=adsl;
   tables trtgrp * Y /cmh /*general association test*/
run;
```

   b) CMH test for ordinal variable (Y), the p-value from row mean score test should be used for ordinal variable:

```
cproc freq order=adsl;
  tables trtgrp * Y / cmh2 ; /*row mean score test*/
run;
```

   c) Wilcoxon rank sum test for continuous variable (Y), the p-value from the normal approximation two-sided test should be used for continuous variable:

```
proc npar1way wilcoxon data=adsl;
   class trtgrp;
   var Y;
run;
```

9) Please note, “Not Permitted”, “Unknown”, or missing categories will be excluded percentage calculation and also excluded for 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.

10) SAS code for treatment comparison for duration of exposure. The p-value from log rank test should be used.

```
proc lifetest data=ADSL method=km;
    time TRTDURD*ESDD(0); /*Derive ESDD from COMT01FL, where ESDD = 0
    indicates censored observation (ie, subject is still on study drug)*/
    Strata TRT01AN;
    label TRTDURD = "Duration of Exposure (Days)";
run;
```

11) Last Dose Date and Last Study Date

a) Last Dose Date (ie, TRTEDTC, TRTEDT, TR01EDT or TR01EDTC) in ADSL was defined in SAP Section 3.8.1.

For subjects with a partial last dosing date (ie, month and year of last dose are known), the latest of the dispensing dates of study drug bottles, study drug start dates and end dates, 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.

Last dose date is not defined for subjects still on study drug in SAP. However, for the calculation of the duration of exposure to study drug, the data cut date will be used to impute the last dose date for subjects who have not permanently discontinued study drug at the time of the data cut date (ie, CRF data cut date from the data cut plan).

For Week 48 interim analysis, 04/26/2017 will be the data cut date for subjects with Week 48 visits on or prior to 04/26/2017, subjects missing week 48 visits while on study drug or subjects prematurely discontinued study drug. For subjects with Week 48 visit after 04/26/2017 but before data finalization, the last Week 48 visit date will be used as the data cut date as appropriate.

b) Last Study Date is the latest of the study drug start dates and end dates, the clinic visit dates, and the laboratory visit dates, including the 30-day follow-up visit date, for subjects who prematurely discontinued study or who completed study according to the Study Completion eCRF. If study drug start date or end date 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 date) and before the imputed last study date, the complete death date should be used as the imputed last study date.

Last study date is not defined for subjects still on study in SAP. However, for programing purpose, the latest of data cut date (ie, CRF data cut date from the data cut plan), the clinic visit dates, and the laboratory visit dates, including the 30-day follow-up visit date, will be used to impute the last study date for subjects still on study.

12) Toxicity Grades:

a) For toxicity grade summaries, include all post-baseline graded results up to 30 days after the last dose of study drug, 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.

13) Efficacy analyses:

a) For categorical efficacy response (eg, Subjects with HIV-1 RNA < 50 copies/mL or Subjects with HIV-1 RNA ≥ 50 copies/mL as determined by US FDA-defined snapshot algorithm, M=F, or M=E Analyses): the proportion difference between two treatment groups and its 95.002% CIs (for HIV-1 RNA < 50 at wk48 by snapshot algorithm for FAS or Week 48 PP set) or 95% CIs are calculated based on the an unconditional exact method using 2 inverted 1-sided tests in SAS v9.3 or above.

b) The following SAS code will be used to compute cell counts and p-value.

```
data example;
input  grp trt01a $  outcome $ count ;

datalines;
1       Treat-A        2-Fail        1
1       Treat-A        1-Succ      189
1       Treat-B        2-Fail        4
1       Treat-B        1-Succ       88
run;

proc freq data = example;
table trt01a*outcome /riskdiff(CL=(exact)) alpha=0.04998;
weight count; exact RISKDIFF(METHOD=SCORE);
output out=ciexact(keep=_RDIF1_ XL_RDIF1 XU_RDIF1 _RSK11_  _RSK21) riskdiff;
run;
```

```
c
data final(keep=A1 B1 Estimate LowerCL UpperCL ocharc1);
set ciexact;
label Estimate ="Percentage Difference"
LowerCL = "95% Lower Confidence Limit"
UpperCL = "95% Upper Confidence Limit"
A1 = "Percentage of Success in Treat-A"
B1 = "Percentage of Success in Treat-B";
Estimate=100*_RDIF1_;
LowerCL = 100*XL_RDIF1;
UpperCL = 100*XU_RDIF1;
A1 = 100*_RSK11_;
B1 = 100*_RSK21_;
ocharc1 = right(compress(put(Estimate,8.1)) || '% (' || compress(put(LowerCL,8.1)) || '%
to ' || compress(put(UpperCL,8.1)) || '%)');
run;
```

c) Please note, alpha=0.04998 is only used for the primary efficacy endpoint (HIV-1 RNA >= 50 c/mL by snapshot algorithm at Week 48) to obtain 95.002% CIs and the endpoint of subjects with HIV-1 RNA < 50 c/mL by snapshot algorithm at Week 48 in FAS and Week48 PP analysis set; otherwise, for the efficacy endpoints with proportions, the alpha=0.05 is used to obtain 95% CIs.

d) The 95% CI for percentage estimate of HIV-1 RNA < 50 copies/mL for each treatment is calculated based on the Clopper-Pearson exact method.

e) Fisher's exact test for categorical efficacy response (eg, HIV-1 RNA < 50 copies/mL by US FDA-defined snapshot algorithm), where *trtgrp* is the treatment, and *response* is the categorical efficacy response. P-value from 2-sided Fisher's exact test should be used to test superiority.

```
proc freq data=adeff;
   tables trtgrp*response/fisher; /*p value from Fisher's exact test*/
run;
```

f) Homogeneity test: Homogeneity Test of Treatment Effect (HIV-1 RNA < 50 copies/mL by US FDA-defined snapshot algorithm) Across Region in HIV-1 RNA < 50 copies/mL at Week 48 (Snapshot Algorithm). For each region, the odds ratio and its 95% CI are calculated from the CMH test. For overall, the odds ratio and its 95% CI are calculated based on the common odds ratio estimate from the CMH test. The p-value for the homogeneity test is based on the Breslow-Day test of the interaction between region and treatment group as follows.

```
proc freq data=xxx;
   tables region*trtgrp* response /all; /*p value from Breslow Day test,
   (trtgrp: 1, 2; response: 1: < 50, 2: >=50)*/
run;
```

g) Subgroup analyses for HIV-1 RNA < 50 copies/mL by US FDA-defined snapshot algorithm

For the subgroups of age, sex, race, baseline CD4 cell count, and study drug adherence, the proportion difference between two treatment groups and its 95% CIs are calculated based on an unconditional exact method using 2 inverted 1-sided tests, similarly to that for the primary efficacy endpoint.

h) Homogeneity test: Homogeneity Test of Treatment Effect (HIV-1 RNA < 50 copies/mL by US FDA-defined snapshot algorithm) between Subgroups in HIV-1 RNA < 50 copies/mL at Week 48 (Snapshot Algorithm)

a. For the subgroups of age, sex, race, region and study drug adherence, the odds ratio and the associated 95% CIs are estimated for the response variable (response; coded as 1 for success and 0 for non-success) using a logistic regression model including subgroup factor (coded as 1 for the first subgroup and 2 for the second subgroup), treatment (trtgrp; coded as 1 for active [ie, B/F/TAF] and 2 for control), and treatment by subgroup factor.

eg. region stratum (region; coded as 1 for “US” and 2 for “Ex-US”)

For example, for the age subgroup (agegrp; coded as 1 for < 50 and 2 for >= 50), the following SAS code will be used to generate the Odds Ratio and its 95% CI within the subgroup:

Note: For the following code, it is assumed that none of the variables have any formats applied to them. If they do, they must be removed before calling the code.

e.g. for the age subgroup, the following codes will be used to get Odds Ratio and 95% CI within subgroup:

```
proc genmod data=data descending;     /*model for success*/
    class trtgrpn agegrp;
    model response = trtgrpn agegrp trtgrpn*agegrp/dist=bin
    link=logit lrci;
    estimate 'Group 1' trtgrpn 1 -1 trtgrpn*agegrp 1 0 -1 0/exp;
    estimate 'Group 2' trtgrpn 1 -1 trtgrpn*agegrp 0 1 0 -1/exp;
run;
```

Note: trtgrpn is the numeric treatment group variable, response is the response outcome variable (1 vs 0 (’<50’ vs’>=50’)), agegrp is the subgroup variable for age (1:< 50 vs 2: >= 50).

(P-value for the homogeneity test was based on the Wald test of the interaction between treatment and subgroup. Odds ratio is from L'Beta estimate, its 95%CI is from L'Beta confidence limits for each subgroup.)

i) ANOVA model for continuous efficacy variable (eg, CD4): The differences in changes from baseline in CD4 cell count between treatment groups and the associated 95% CI will be constructed using an ANOVA, including treatment as fixed effect in the model.

```
proc glm data=adeff;
   class trtgrp;
   model CD4=trtgrp;
   lsmeans trtgrp /alpha=0.05 cl pdiff;
run;
```

j) Listing for US FDA-defined snapshot outcome:

In addition to flagging the values of HIV-1 RNA < 50 or ≥ 50 copies/mL for virologic outcomes, flag the last available HIV-1 RNA value while on treatment for the following categories:

i) HIV-1 RNA >= 50 copies/mL - Discontinued Study Drug Due to AE or Death and Last Available HIV-1 RNA >= 50 copies/mL

ii) HIV-1 RNA >= 50 copies/mL - Discontinued Study Drug Due to Other reason* and Last Available HIV-1 RNA >= 50 copies/mL

iii) No virologic Data – Discontinued Study Drug Due to AE or Death and Last Available HIV-1 RNA < 50 copies/mL

iv) No virologic Data – Discontinued Study Drug Due to Other reason* and Last Available HIV-1 RNA < 50 copies/mL

Note: * Other reasons include subjects who discontinued study drug due to investigator's discretion, subject decision, lost to follow-up, noncompliance with study drug, protocol violation, pregnancy, and study terminated by sponsor.

14) DXA Analysis:

a) Variable used for analysis:

i) Variable CORRBMD when Region = "SpineTotalAdequate" for spine, Region = "FemurTotal" for hip, and Region = "FemurNeck" for femur neck will be used for percentage change from baseline in BMD analysis.

ii) Variable CORRTSCR when Region = "SpineTotalAdequate" for spine and Region = "FemurTotal" for hip will be used for defining the BMD clinical status.

b) BMD clinical status comparison: Rank Analysis of covariance

base is the baseline BMD clinical status and *post* is the post baseline clinical status (both coded as 0 for normal, 1 for Osteopenia, 2 for Osteoporosis, . for missing). The p-value from row mean score test from the last proc freq procedure is the p-value for rank analysis of covariance.

```
proc rank data=addxa nplus1 ties=mean out=ranks1;
   var base post;
   rank baserank postrank;
run;

proc reg data=ranks1;
   model postrank=baserank;
   output out=residual1 r=resid;
run;

proc freq data=residual1;
   tables trtgrp*resid/noprint cmh2; /* row mean score test*/
run;
```

15) For gradation categories of percentage change from baseline in the hip BMD and spine, the distribution difference in these categories between the treatment groups will be compared using CMH test (row mean scores differ statistic).

```
SAS codes for treatment comparison will be:

proc freq order=data;
   tables trtgrp * Y / cmh2 ; /*row mean score test*/
run;
```

16) Clarification of the following LOCF algorithms:

- Baseline values will be carried forward.
- For CD4:

  If a value is missing in an analysis visit window, replace the missing value with the last on- treatment value observed before the analysis visit window that has the missing value.

- For DXA BMD:

  If a value is missing in an analysis visit window, the missing value will be replaced with the last value observed before the analysis visit window that has the missing value.

17) For safety ECGs at postbaseline visits, the most conservative (worst) value within the window will be selected, eg, abnormal will be selected over normal for safety ECG or clinical significant abnormal will be selected over not clinical significant abnormal if there are multiple abnormal findings.

18) TEAE

Events with Missing Onset Day and/or Month

An event 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.

19) 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)
	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	Increase	N/A
	Urine Glucose	Increase	Urine Glucose (Glycosuria)
	Urine Protein	Increase	Urine Protein (Proteinuria)
	Urine RBC	Increase	Urine RBC (Hematuria, Quantitative)

20) Renal related laboratory evaluation

a) Unit conversion for renal safety tests derived from related tests with conventional units

- Urine RBP (ug/L) to creatinine (mg/dL) ratio: 1 (ug/L) / (mg/dL) = 100 × ug/g
- Urine Beta-2-microglobulin (mg/L) to creatinine (mg/dL) ratio: 1 (mg/L) / (mg/dL) = 10^5 ug/g
- Urine Albumin (mg/dL) to creatinine (mg/dL) ratio: 1 (mg/dL) / (mg/dL) = 1000 × mg/g

b) Calculation of ratios:

To calculate laboratory ratios (eg, urine RBP to creatinine ratio), lab value of each test in the ratio needs to be from the same accession number; if any test value used for the ratio calculation from the same accession number is missing , the ratio is not calculable (ie, missing).

21) Medical history of interest at baseline

Medical history of diabetes, hypertension, cardiovascular disease, and hyperlipidemia will be summarized as baseline disease characteristics. A subject who had medical history of one of these diseases is a subject who experienced at least one of the following: selected medical history, selected AE preferred terms or selected concomitant medications with start date prior to or on the first dose date.

22) Smoking status at baseline

Smoking status at baseline (ie, never smoker, former smoker, and current smoker) will be summarized as part of the baseline disease characteristics.

Former smoker at baseline refers to the subjects who has stopped the use of any Cigarettes or Cigars before study day 1 (ie, the first dose date).

Current Smoker at baseline refers to the smokers who has use of any Cigarettes or Cigars at study day 1.

Never smoker at baseline refers to subjects who have no record with Type of Substance Use = “Cigarettes” or “Cigars” on or prior to study day 1.

How to classify a subject as never smoker, former smoker, or current smoker at baseline is specified as follows:

a) First select only records with *Type of Substance Use* = "Cigarettes" or "Cigars". Records with *Type of Substance Use* = "Other" (including chew tobacco, e-cigarettes, etc) will not be considered as smoking.

b) Second, for each selected substance use record, flag whether it is "Prior", "Present", or "Post" relative to the first dose date according to the algorithm below.

c) Finally, (1) the subject will be flagged as "Never" smoker, if the subject has no record with *Type of Substance Use* = "Cigarettes" or "Cigars" or all selected records have a flag of "Post"; (2) the subject will be flagged as a "Former" smoker, if any selected record has flag of "Prior" and no record of "Present"; (3) Otherwise, the subject will be flagged as a "Current" smoker, if any selected records has a flag of "Present".

	Selected Substance Use Records							
Prior	No	No	Yes	Yes	Yes	No	No	Yes
Present	No	No	No	No	Yes	Yes	Yes	Yes
Post	No	Yes	No	Yes	No	No	Yes	Yes
Smoking Status	Never	Never	Former	Former	Current	Current	Current	Current

Algorithm to flag whether a selected record is "Prior", "Present", or "Post" relative to the first dose date:

1. The start and stop dates of the selected record are not completely missing (ie, at least year is known) or the start date is not missing and record is ongoing. The complete start or stop dates will be used to compare with the first dose date whenever possible. Otherwise, the month and year (or year alone if month is not recorded) of the start or stop dates will be used to compare with the first dose date when the start or stop date of the selected record is incomplete:

    a) The record is flagged as "Prior", if the stop date is before the first dose date;

    b) The record is flagged as "Present", if the start date is on or beforer the first dose date and the stop date is on or after the first dose date, or the selected record is marked as ongoing and the start date is on or before the first dose date;

    c) The record is flagged as "Post", if the start date is after the first dose date

2. The start date of the selected record is completely missing. We assume that the start date is before the first dose date, the stop date (or the month and/or year of the stop date, if stop date is incomplete) or "ongoing" will be used to determine whether the selected record is "Prior" or "Present" as follows:

   a) The record is flagged as "Prior", if the stop date is before the first dose date or the stop date is completed missing and the record is not marked as ongoing.

   b) The record is flagged as "Present", if the stop date is on or after the first dose date or the selected record is marked as ongoing.

3. The start date of the selected record is before the first dose date, but the stop date is completely missing and the record is not marked as ongoing. We assume that the end date is before the first dose date, the record is flagged as "Prior".

4. The start date of the selected record is on or after the first dose date, but the stop date is completely missing and the record is not marked as ongoing. This is a data issue, should be queried first. However, this record is flagged as "Present" if the start date is on the first dose; this record is flagged as "Post" if the start date is after the first dose.

23) Clarification for "Pharmacokinetic Blood Sampling Time Record" listing

- A new variable "Sample age" will be added in this listing, defined as the duration in day between sample collection date and assay date, ie, sample age = assay date – sample collection date + 1.

- SAMTIME (hours) = sample collection time (xx:xx) - last dose time before sample collection (xx:xx).

  Except for SAMTIME for intensive PK samples at predose:

  SAMTIME (hours) = predose sample collection time (xx:xx) - dose time after predose sample collection (xx:xx).

  Note: please round the SAMTIME to 1 decimal place, and then using **20.0** <=SAMTIME<= **28.0** hours criteria to flag trough samples. In l-pk listing, please display 1 decimal place for SAMTIME.

24) PK parameters at the individual subject level should be displayed with the following reported number of decimal places:

- LambdaZ, r2, r2 adj, and CORRXY: 3 decimal places

- $t_{1/2}$, T_{last}, T_{max}, BEGHOUR, and ENDHOUR: 2 decimal places

- AUC_{tau}, $AUC_{0\text{-}last}$, AUC_{inf}, $\%AUC_{exp}$, Vz/F, CL/F, CLss/F, C_{max}, C_{last} and C_{tau}: 1 decimal place

- NPOINTS: 0 decimal place

PK concentration data will be reported with 1 decimal place.

25) PK parameters included in PK summary tables are defined in PK aberration listing, except that TAF C_{tau} will not be included in corresponding PK summary table, since TAF C_{tau} should be BLQ for all subjects due to the short half-life of TAF.

- PK parameters should be displayed as alphabetic order as listed in PK abbreviation listing.

- SDTM.PP.PPSPID should be used as the label for each PK parameter, which also listed in PK abbreviation listing.

26) Concomitant nonstudy-drug ARV medications (ie, ARV medications other than study drug that are taken while receiving study drug) 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 7.5.2)

27) Lipid modifying medication analyses:

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

- Subjects who took lipid modifying medications at study entry refer to the subjects who has any use of the lipid modifying agents at study day 1 (ie, the first dose date).

  a) More specifically, subjects with "Lipid Modifying Agent Use at Study Entry" include those subjects in safety analysis set with meeting both the following criteria: 1) any selected CM record with the start date ≤ the first dose date, and 2) the end date of the selected CM record ≥ the first dose date or the end date of the selected CM record is ongoing

  b) For lipid modifying medications with the start date completely unknown, we assume the start date is on or before the first dose date, lipid modifying medication was considered as being taken at study entry if the end date is not prior to the first dose date (ie, the end date is on or after the first dose date, completely unknown, or ongoing).

  c) Lipid modifying medications with the start date prior to the first dose date and the end date unknown (completely missing) were considered as being taken at study entry (the unknown end date is assumed on or after the first dose date).

- Subjects who initiated lipid modifying medications during the study refer to the subjects in the safety analysis set who didn't take lipid modifying medications at study entry and met the following criteria: 1) for subjects who permanently discontinued study drug with any selected CM record started after the first dose date and on and prior to the last dose date; 2) for subjects who are still on study drug with any selected CM records first started after the first dose date.

28) 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.

29) Vital signs and weight, height, BMI will be in the same listing.

30) 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	CNT63	Hep B Surface Ag	"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, when considering the different laboratory tests, take the latest, non-missing record on or prior to the first dose date 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 and on or prior to the last dose date

  — For incomplete AE start dates, please follow the logic specified in Section 7.1.4.2, 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".

31) 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.

32) For exclusion criteria for subjects in Per protocol set who were excluded from full analysis set:

- Subjects who do not meet the inclusion criterion of being on a stable regimen for ≥ 3 months preceding the screening visit with documented plasma HIV-1 RNA < 50 copies/mL for ≥ 3 months preceding the Screening visit (or undetectable HIV-1 RNA level according to the local assay being used if the limit of detection is ≥ 50 copies/mL).

  The above subjects include subjects do not meet inclusion criteria 15 in both original protocol and protocol amendment 1.

  Inclusion criteria 15 in original protocol: Currently on the first or second ARV regimen with documented plasma HIV-1 RNA < 50 copies/mL on a stable regimen for ≥ 3 months preceding the Screening visit.

  Inclusion criteria 15 in protocol amendment 1: Currently on a stable regimen for ≥ 3 months preceding the screening visit with documented plasma HIV-1 RNA < 50 copies/mL for ≥ 3 months preceding the Screening visit (or undetectable HIV-1 RNA level according to the local assay being used if the limit of detection is ≥ 50 copies/mL).

33) Reasons for Subjects who excluded from Week 48 PP Analysis Set will be summarized as follows in table:

a) Did Not Have On-Treatment HIV-1 RNA in Week 48 Window Unless due to Discontinuation of Study Drug for Lack of Efficacy

b) Did Not Meet the Criteria of Taking DTG + ABC/3TC, or ABC/DTG/3TC FDC for >= 3 Months Before Screening Visit

c) Did Not Meet the Criteria of HIV-1 RNA < 50 copies/mL for >= 3 months before Screening visit

d) Did Not Meet the Criteria of Having no Resistance to any component of study regimen

e) Did Not Meet the Criteria of HIV-1 RNA < 50 copies/mL at Screening Visit

f) Took Protocol Prohibited Medications

g) Adherence Rate for Active Study Drug up to Week 48 Visit Below the 2.5th

34) The number of decimal places in reporting p-values should be as follows:

a) values less than 0.001 → < 0.001

b) values 0.001 to less than 0.10 → round to 3 decimal places

c) values 0.10 and greater → round to 2 decimal places