STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 3, Randomized, Open Label Study to Evaluate the Safety and Efficacy of Switching to a Fixed Dose Combination (FDC) of GS-9883/Emtricitabine/Tenofovir Alafenamide (GS-9883/F/TAF) from Elvitegravir/Cobicistat/Emtricitabine/ Tenofovir Alafenamide (E/C/F/TAF), Elvitegravir/Cobicistat/ Emtricitabine/Tenofovir Disoproxil Fumarate (E/C/F/TDF) or Atazanavir + Ritonavir + Emtricitabine/Tenofovir Disoproxil Fumarate (ATV+RTV+FTC/TDF) in Virologically Suppressed HIV-1 Infected Women
Name of Test Drug:	Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF; GS-9883/F/TAF)
Study Number:	GS-US-380-1961
Protocol Version (Date):	Amendment 2 (10 November 2016)
Analysis Type:	Week 48 Interim Analysis
Analysis Plan Version:	Version 1.0
Analysis Plan Date:	19 October 2017
Analysis Plan Author(s):	PPD

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LIST OF ABBREVIATIONS

AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
ANOVA	analysis of variance
ARV	antiretroviral
AST	aspartate aminotransferase
ATV	Atazanavir
B2M	beta-2 microglobulin
BIC	Bictegravir, GS-9883, B
B/F/TAF	single-tablet regimen of bictegravir (BIC; B) 50 mg / emtricitabine (FTC) 200 mg / tenofovir alafenamide (TAF) 10 mg; GS-9883/F/TAF
BLQ	below limit of quantitation
BMI	body mass index
BSA	body surface area
CG	Cockroft-Gault
CI	confidence interval
CMH	Cochran-Mantel-Haenszel
CRF	case report form
CSR	clinical study report
DNA	Deoxyribonucleic Acid
DOB	date of birth
DSPH	Drug Safety and Public Health Department
E/C/F/TAF	Elvitegravir /Cobicistat /Emtricitabine/ Tenofovir Alafenamide; Genvoya; GEN
E/C/F/TDF	Elvitegravir /Cobicistat /Emtricitabine / Tenofovir Disoproxil Fumarate; Stribild; STB
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
FTC/TDF	single-tablet regimen of emtricitabine 200 mg/ tenofovir alafenamide 10 mg
FTC	Emtricitabine; F
GFR	glomerular filtration rate
GGT	gamma-glutamyl transferase
Gilead	Gilead Sciences, Inc.
GS-9883	Bictegravir; BIC; B
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	HCV antibody
HDL	high density lipoprotein
HIV-1	human immunodeficiency virus (Type 1)
HLGT	high level group term
HLT	high level term
ID	identification
IDMC	independent data monitoring committee
INR	international normalized ratio
IWRS	interactive web response system
KM	Kaplan-Meier
LDL	low density lipoprotein
LLOQ	lower limit of quantitation
LLT	lowest level term
LOCF	last observation carried forward
MedDRA	Medical Dictionary for Regulatory Activities
MH	Mantel-Haenszel
OLE	open-label extension
PK	pharmacokinetic
PP	per protocol
PT	preferred term
PT	prothrombin time
Q	quartile
Q1	first quartile
Q3	third quartile
RBP	retinol binding protein
RNA	ribonucleic acid
RTV	Ritonavir
SAE	serious adverse events
SAP	statistical analysis plan
SBR	stay on baseline regimen
SD	standard deviation
SE	standard error
SMQ	Standardised MedDRA Query
SOC	system organ class

TAF	tenofovir alafenamide
TEAE	treatment-emergent AE
TFL	tables, figures, and listings
TFV	tenofovir
TSH	thyroid stimulating hormone
ULN	upper limit of normal
UACR	urine albumin to creatinine ratio
WHO	World Health Organization

1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical analysis methods and data presentations to be used in tables, figures, and listings (TFLs) of the Week 48 interim analysis for Study GS-US-380-1961, 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 10 November 2016 and the electronic case report form (eCRF). The SAP will be finalized before data 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 to a fixed dose combination (FDC) of bictegravir (GS-9883; BIC; B) /emtricitabine (FTC; F) /tenofovir alafenamide (TAF) versus continuing on a regimen consisting of E/C/F/TAF, E/C/F/TDF, or ATV+RTV+FTC/TDF in virologically suppressed HIV-1 infected women as determined by the proportion of subject with HIV-1 RNA ≥ 50 copies/mL at Week 48.

The secondary objective of this study is:

- To evaluate the safety and tolerability of the treatment groups through Weeks 48.

1.2. Study Design

Design Configuration and Subject Population

GS-US-380-1961 is a randomized, open label, multicenter, active-controlled study to evaluate the safety and efficacy of switching to an FDC of B/F/TAF in HIV-1 infected women who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a regimen consisting of E/C/F/TAF, E/C/F/TDF, or ATV+RTV+FTC/TDF for ≥ 12 consecutive weeks prior to screening.

All subjects will be HIV-1 infected women drawn from pre-defined Gilead Sciences In. (Gilead) clinical studies and must be virologically suppressed. Women in Gilead study GS-US-236-0128 who completed the Week 48 open-label extension (OLE) visit or any post Week 48 OLE visits, women in study GS-US-292-0109 who completed the Week 96 visit or any post Week 96 visits, or women in studies GS-US-292-0104 or GS-US-292-0111 who completed the Week 144 visit or any post Week 144 visits may be eligible to enroll.

Treatment Groups

Subjects who provide written consent and meet all eligibility criteria will be randomized in a 1:1 ratio to receive open label medication as follows:

Treatment Group 1: FDC of BIC 50 mg/FTC 200 mg/TAF 25 mg (B/F/TAF) administered orally, once daily, without regard to food (approximately n = 235)

Treatment Group 2: Stay on baseline regimen (SBR), including E/C/F/TAF, E/C/F/TDF, or ATV+RTV+FTC/TDF administered orally, once daily, with food (approximately n = 235)

Key Eligibility Criteria

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

- Currently on a stable antiretroviral regimen consisting of E/C/F/TAF, E/C/F/TDF, or ATV+RTV+FTC/TDF continuously for ≥ 12 consecutive weeks preceding the screening visit
- Documented plasma HIV-1 RNA levels < 50 copies/mL for ≥ 12 weeks preceding the Screening visit. After reaching HIV-1 RNA < 50 copies/mL, single values of HIV-1 RNA ≥ 50 copies/mL followed by re-suppression to < 50 copies/mL is allowed
- HIV-1 RNA <50 copies/mL at screening
- Estimated glomerular filtration rate (eGFR) ≥ 50 mL/min according to the Cockcroft-Gault (C-G) formula at the screening visit

Study Periods / Phases

Subjects will be treated for at least 48 weeks. At the Week 48 Visit, subjects in a country where B/F/TAF FDC is not available will be given the option to receive B/F/TAF FDC for an additional 48 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.

Subjects who complete the study through the Week 48 Visit and do not continue participation in the study will be required to return to the clinic 30 days after the Week 48 Visit for a 30 Day Follow-Up 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 Screening and Day 1 visits, subjects will return for study visits at Weeks 4, 8, 12, and then every 12 weeks until the Week 48 visit.

For all eligible subjects, blood and urine will be collected at Day 1, Weeks 4, 8, 12, and then every 12 weeks through the Week 48 visit. Laboratory analyses (including 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.

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

Pharmacokinetics

For all subjects on B/F/TAF (Treatment Group 1), a single anytime pre or post-dose PK blood sample will be collected at Weeks 8, 24, and 36.

For all subjects on B/F/TAF (Treatment Group 1), 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 PK blood sample will be collected between 1 and 4 hours post-dose.

The concentration of BIC may be summarized using descriptive statistics.

Randomization

Subjects will be randomized in a 1:1 ratio to 1 of 2 Treatment Groups (Treatment Group 1: Treatment Group 2). Randomization will be stratified by the prior treatment regimen group (ie, E/C/F/TAF, E/C/F/TDF, and ATV+RTV+FTC/TDF).

Site and/or Stratum Enrollment Limits

Approximately 57 study sites in North America, Dominican Republic, Thailand, Russia, and Uganda participated. There was no enrollment limit for individual sites.

Study Duration

The randomized phase of this study is 48 weeks in duration.

1.3. Sample Size and Power

A total of approximately 470 HIV-1 infected women, randomized in a 1:1 ratio to 2 treatment groups (approximately 235 subjects per treatment group), achieves at least 87% power to detect a non-inferiority margin of 4% difference in the percentage of subjects with HIV-1 RNA $\geq$ 50 copies/mL at Week 48 between the 2 treatment groups.

For sample size and power computation, it is assumed that both treatment groups have 2% of subjects with HIV-1 RNA $\geq$ 50 copies/mL at Week 48 (based on the historical Gilead Genvoya®[GEN; E/C/F/TAF] and Stribild® [STB; E/C/F/TDF] studies), that a 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 Analysis

The Week 24 Independent Data Monitoring Committee (IDMC) analysis was conducted after all subjects enrolled completed their Week 24 visit of the study or prematurely discontinued the study drug. The purpose of this interim analysis 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 result or to consider early termination of the study even if there is early evidence of favorable efficacy for B/F/TAF.

2.2. Week 48 Interim Analysis

The Week 48 interim 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

The Week 48 interim analysis will include all data collected from the randomized and the extension phases of the study. Only data collected in the randomized phase (ie, randomized phase data) will be summarized by treatment group, if not specified otherwise. Data collected from both phases will be included in data listings. Data included in each phase are defined as follows:

Randomized Phase Data

- For subjects who are never treated in the extension phase of the study, all available data are considered as the randomized phase data.
- For subjects treated in the extension phase of the study, randomized phase data are defined as data collected **up to** the extension phase first dose date except for data on adverse events (AEs), concomitant medications, pregnancy, and death. For AEs, concomitant medications, pregnancy, and death, only data collected **prior to** the extension phase first dose date are included.

Extension Phase Data

- Extension phase data are only available from subjects who enter the extension phase of the study. Extension phase data are defined as data collected after the extension phase first dose date except for data on AEs, concomitant medications, pregnancy, and death. For AEs, concomitant medications, pregnancy, and death, data collected on or after the extension phase first dose date are included.

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 the randomized study drug refers to premature discontinuation of the randomized study drug or completion of the randomized study drug. Similarly, permanent discontinuation of the extension study drug refers to premature discontinuation of the extension study drug or completion of the extension 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 data finalization. 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 randomized study drug. Subjects will be grouped according to the treatment to which they were randomized. For the FAS, all randomized phase efficacy data 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 randomized 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, randomized phase efficacy data collected up to 1 day after the randomized phase last dose date 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 an 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 on the Randomized Phase 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 criteria for no documented or suspected resistance to FTC, TFV, ATV, or EVG, including but not limited to the reverse transcriptase resistance mutations K65R and M184V/I.

- Subjects who meet the exclusion criterion for receiving ongoing therapy with any of the medications listed in Tables 5-1 and 5-2 in protocol Section 5.4.

- 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 randomized study drug. All randomized phase safety data collected up to 30 days from the randomized phase last dose date 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. Pharmacokinetic (PK) Analysis Set

The **PK Analysis Set** will include all subjects who (1) are randomized into the B/F/TAF treatment group, (2) have received at least 1 dose of B/F/TAF in the randomized phase of the study, 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.

3.2. 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 analysis.

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 (see Section 6.2.2.2 for details):

- Age (years): (a) < 50 and (b) ≥ 50
- 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)

The proportion of subjects with hepatitis B virus (HBV) Deoxyribonucleic Acid (DNA) < 29 IU/mL at baseline and Week 48, and the change from baseline in $\log_{10}$ HBV DNA by visit will be analyzed for the following subject subgroup:

- Subjects with HIV/HBV coinfection at baseline

3.4.2. Subject Subgroups for Safety Analyses

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

- Age (years): (a) < 50 and (b) ≥ 50
- 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 HIV/HBV coinfection at baseline
- Subjects with incident HIV/HBV coinfection while on study drug (if any)

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

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

Lastly, subgroup analysis by prior treatment regimen (ie, TDF-containing regimen versus non-TDF containing regimen) will be performed for the following endpoints:

- Urine retinal binding protein (RBP) to creatinine ratio
- beta-2 microglobulin to creatinine ratio
- Urine albumin to creatinine ratio (UACR)

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 the US FDA-defined snapshot algorithm was the prespecified primary comparison. However, the Week 24 interim IDMC analysis was performed prior to the analysis for the primary endpoint and an alpha penalty of 0.00001 was applied for the Week 24 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 0.04999 (corresponding to 95.001% 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 determined by the US FDA-defined snapshot algorithm, will also be adjusted to 0.04999 (corresponding to 95.001% CI) to be conservative using both the FAS and the Week 48 PP analysis set. No alpha level adjustment is applied other than for the primary and key secondary endpoints listed above.

3.6. Missing Data and Outliers

3.6.1. Missing Data

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

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

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

For missing last dosing date of study drug, imputation rules are described in Section 3.8.1. The handling of missing or incomplete dates for AE onset is described in Section 7.1.5.2, and for concomitant non-antiretroviral (ARV) medications in Section 7.4.3.

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.

Logarithm (base 10) transformation will be applied to HIV-1 RNA and HBV DNA data for efficacy analysis. 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 purpose. HBV DNA results of "<20 IU/mL HBV DNA detected" or "No HBV DNA detected" will be imputed as 19 IU/mL for analysis purpose. HCV RNA results of "<15 IU/mL HCV RNA detected" or "No HCV RNA detected" will be imputed as 14 IU/mL for analysis purpose.

Natural logarithm transformation will be used for analyzing concentrations in plasma samples. Concentration values that are below the lower limit of quantitation (BLQ) will be presented as "BLQ" in the concentration listing.

3.8. Analysis Windows

3.8.1. Definition of Study Day

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

Study Day 1 (Extension Phase) is defined as the day when the first dose of extension phase study drug (ie, *B/F/TAF)* was taken, as recorded on the "Extension Phase" Study Drug Administration eCRF. This day will only be available for subjects treated in the extension phase of the study.

Study Days are calculated relative to randomized phase Study Day 1. For events that occurred on or after the randomized phase Study Day 1, study days are calculated as (visit date minus randomized phase Study Day 1 plus 1). For events that occurred prior to the randomized phase Study Day 1, study days are calculated as (visit date minus randomized phase Study Day 1). All study days will be calculated from randomized phase Study Day 1 including observations collected from the extension phase of the study.

Last Dose Date (Randomized Phase) is defined as the latest of the randomized study drug end dates recorded on the "Randomized Phase" Study Drug Administration eCRF with "Permanently withdrawn" box checked for subjects who prematurely discontinued or completed the randomized study drug in the "Randomized Phase" according to the Study Drug Completion eCRF.

If the last dose date for randomized phase is missing (eg, only year of last dose date is known or completely missing due to lost to follow-up) for subjects who prematurely discontinued study drug or completed the study drug at the data cut date, the latest of nonmissing randomized 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, from the randomized phase data, will be used to impute the randomized phase last dose date. For other partial missing last dose date, please see programming specification for imputation rule details. For subjects who are still on the randomized phase study drug, the data cut date will be used to impute the last dose date.

Last Dose Date (Extension Phase) is defined as the latest of the extension phase study drug end dates recorded on the "Extension Phase" Study Drug Administration eCRF with "Permanently Withdrawn" box checked for subjects who prematurely discontinued study drug according to the "Extension Phase" Study Drug Completion eCRF. This date will only be available for subjects treated in the extension phase of the study.

If the last dose date is missing for subjects who prematurely discontinued study drug in the extension phase of the study, the latest of nonmissing extension phase 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, from the extension phase data, will be used to impute the extension phase last dose date. For subjects who are still on the extension phase study drug, the data cut date will be used to impute the last dose date.

Last Study Date is the latest of the randomized or extension phase (if available) study drug start dates and end dates, the clinic visit dates, and the laboratory visit dates, including the 30-day follow-up visit date, for subjects who prematurely discontinued study or who completed study according to the Study Completion eCRF. For subjects still on study, the last study date is defined to be the latest of data cut date, the clinic visit dates, and the laboratory visit dates, including the 30-day follow-up visit date. 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.

Baseline value is defined as the last value obtained on or prior to the randomized phase Study Day 1 for all assessments.

3.8.2. Analysis Windows

Subject visits might not occur on protocol specified days. Therefore, for the purpose of analysis, observations collected from the randomized phase of the study (ie, randomized phase data) will be assigned to analysis window. Observations collected from the extension phase of the study (ie, extension phase data) will not have analysis window assigned and will be included in listings with derived visit marked as "Extension". Any observations from the randomized phase in the "Post Week 48" window defined in Tables 3-2 to 3-5 will not be summarized in tables and figures, but included in listings.

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

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

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
Post Week 48	NA	379	

Note: HBV DNA collection schedules are as follows: (1) For subjects who meet the definition of HBV infection at screening, HBV DNA will be collected at baseline, Weeks 4, 8, 12, 24, 36, and 48. (2) For subjects who meet the definition of HBV infection at any postbaseline visit, HBV DNA test will be performed at all subsequent visits. (3) For subjects who do not meet the definition of HBV infection at any visit, HBV DNA will be collected at baseline and Week 48.

The analysis windows for metabolic assessments (including fasting glucose and lipid panel: total cholesterol, high density lipoprotein [HDL], direct low density lipoprotein [LDL], triglycerides, and total cholesterol to HDL ratio) and HBV serology (including hepatitis B surface antibody [HBsAb], hepatitis B surface antigen [HBsAg], hepatitis B e-antigen [HBeAg], hepatitis B e-antibody [HBeAb], and hepatitis B core antibody [HBcAb]) are presented in Table 3-3.

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

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
Post Week 48	NA	421	

Note: HBV serology collection schedules are as follows: (1) For subjects who meet the definition of HBV infection at screening, HBV serology will be collected at Weeks 12, 24, and Week 48. (2) For subjects who meet the definition of HBV infection at any postbaseline visit, HBV serology will be performed at all subsequent visits. (3) For subjects who do not meet the definition of HBV infection at any visit, HBV serology will be collected at baseline and Week 48.

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

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

Visit ID	Nominal Day	Lower Limit	Upper Limit
Baseline			1
Week 24	168	2	252
Week 48	336	253	420
Post Week 48	NA	421	

The analysis windows for HCV serology and HCV RNA assessments are presented in Table 3-5.

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

Visit ID	Nominal Day	Lower Limit	Upper Limit
Baseline			1
Week 48	336	2	504
Post Week 48	NA	505	

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 collected from the randomized phase of the study will be chosen as follows:

- For baseline, the latest available record on or prior to the first dose date of randomized study drug will be selected. If there are multiple records with the same collection time or no collection time recorded on the same day, average will be used for the baseline value, except for HIV-1 RNA (see below).

- For postbaseline visits:

  — For CD4+ cell count, CD4%, and HBV DNA, the record(s) collected on the latest day in the window will be selected for analysis.

  — For other numeric observations (eg, except HIV-1 RNA, CD4+ cell count, CD4%, and HBV DNA), the record(s) collected on the day closest to the nominal day for that visit will be selected. If there are 2 days equidistant from the nominal day, the later day will be selected.

  — For any numeric observations except HIV-1 RNA, if there are multiple records on the selected day, the arithmetic mean will be used.

- For baseline and postbaseline HIV-1 RNA, the latest (considering both collection 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 randomized study drug will be selected. If there are multiple records with the same collection time or no collection 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 country, and investigator will be summarized by treatment group and overall using safety analysis set. The denominator for this calculation will be the number of subjects in the safety analysis set. Similarly, the number and percentage of subjects enrolled in each randomization stratum will be summarized using stratum assignment captured in the interactive web response system (IWRS).

If there are discrepancies between IWRS and ARV data with regard to stratum assignment, a listing of the discrepancies will be provided.

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 FAS.

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

- Still on study drug in the randomized phase, if applicable
- Completing study drug in the randomized phase
- Prematurely discontinuing study drug in the randomized phase (with summary of reasons for discontinuing study drug)
- Still on study in the randomized phase, if applicable
- Completing study in the randomized phase
- Prematurely discontinuing from study in the randomized phase (with summary of reasons for discontinuing study)
- Entering and treated in the extension phase
- Subjects still on study drug in the extension phase
- Prematurely discontinuing study drug in the extension phase

The denominator for the percentages of subjects in each category, except for the categories of "subjects still on study drug in the extension phase" and "prematurely discontinuing study drug in the extension phase", will be the number of subjects in the safety analysis set. The denominator for the percentage of subjects in the categories of "subjects still on study drug in the extension phase" and "prematurely discontinuing study drug in the extension phase" will be the numbers of subjects entering and treated in the extension phase.

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 Randomized Study Drug

Duration of exposure to randomized study drug is defined as (the randomized phase last dose date – the randomized phase 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 the randomized phase of the study at the time of the data cut date.

Duration of exposure to randomized 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), etc.

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

Time to premature discontinuation of randomized study drug will be analyzed using the Kaplan-Meier (KM) 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 randomized treatment groups. Subjects who completed 48-week randomized phase of the study treatment will be censored at the last dose date of the randomized study drug. Subjects who are still on the randomized study drug will be censored at the imputed last dose date (ie, data cut date). A plot of KM estimates for the time to premature discontinuation of the randomized 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 of each randomized study drug included in that study drug regimen. The numbers of pills of randomized phase study drug (ie, B/F/TAF, GEN, STB, ATV, RTV, or FTC/TDF) dispensed and returned are captured on study drug accountability eCRF.

Adherence (%) of a study drug regimen (Note: study drug regimen only includes 1 study drug for B/F/TAF, GEN, STB, and 3 study drugs for ATV+RTV+FTC/TDF) will be calculated as follows for pills dispensed in the randomized phase of the study:

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

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

[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 of the same dispensing date, 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 for each study drug contained in the study drug regimen 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 of the same dispensing date. Total number of pills prescribed is determined by summing the number of pills prescribed for each study drug contained in the study drug regimen 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 the same dispensing period for the study drug, (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, all records in that dispensing period for that study drug will be excluded from both denominator and numerator calculation.

Adherence up to Week 48 visit (ie, overall adherence for the randomized phase of the study) will be calculated using all data from the entire dosing period up to the date of permanent discontinuation of the randomized study drugs.

Descriptive statistics for 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 randomized phase of 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 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:

- 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 Appendix 3 for details)
- HIV/HBV coinfection status (Yes/No/Missing, see Section 9.1 for definition)
- HIV/HCV coinfection status (Yes/No/Missing, see Section 9.2 for definition)
- Smoking status: (a) Never Smoker, (b) Former Smoker, and (c) Current Smoker (see Appendix 5 for details)
- Prior ARV regimen: (a) E/C/F/TAF, (b) E/C/F/TDF; (c) RTV boosted ATV + FTC/TDF (see Section 7.4.2 and Appendix 5 for details)

For categorical data, the Cochran-Mantel-Haenszel (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 purposes.

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 to1 day after the randomized phase last dose date) 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 naive 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 SBR 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 SBR 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 SBR. Noninferiority will be assessed using a conventional 95% CI approach, with a noninferiority margin of 4%.

For the interim analysis performed for the IDMC at Week 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 0.04999 (corresponding to 95.001% CI).

The point estimate of treatment difference (B/F/TAF group – SBR group) in the percentage of subjects with HIV-1 RNA ≥ 50 copies/mL and the associated 2-sided 95.001% 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 SBR if the upper bound of the 2-sided 95.001% CI of the difference (B/F/TAF group – SBR 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 SBR is established, the same 95.001% CI used in evaluating noninferiority at Week 48 will be used to evaluate superiority. If the upper bound of the 95.001% CI is less than 0, superiority of B/F/TAF over SBR 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, 95.001% CI for the treatment difference in the primary efficacy endpoint will also be evaluated 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

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 as determined by the US FDA-defined snapshot algorithm will be analyzed similarly to the primary efficacy endpoint. However, the noninferiority margin used for this endpoint 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/TAF group – SBR group) in the percentage of subjects with HIV-1 RNA < 50 copies/mL and the associated 2-sided 95.001% 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 SBR if the lower bound of the 2-sided 95.001% CI of the difference between treatment groups (B/F/TAF group – SBR 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 Week 48 PP analysis set.

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

For each country, 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 country and overall. The homogeneity of the odds ratios across different countries 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/mL as Determined by US FDA-defined Snapshot Algorithm

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 factor, treatment, and treatment by subgroup factor. 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 the randomized phase last dose date) for subjects in the FAS and in the Week 48 PP analysis set, respectively.

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. The change from baseline in CD4+ cell count will also be summarized at visits other than Week 48 by treatment group.

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 the randomized phase last dose date) 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 nonmissing 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

PPD

PPD

PPD [redacted]

6.4. Changes From Protocol-Specified Efficacy Analyses

No change from protocol-specified efficacy analysis is planned.

7. SAFETY ANALYSES

Safety data from the randomized phase of the study (ie, randomized phase data) will be summarized for the subjects in the safety analysis set. All safety data collected up to 30 days after the randomized phase last dose date will be summarized by treatment group, unless specified otherwise. All safety data from both phases of the study 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 lower-level term (LLT) will be provided in the AE dataset.

7.1.2. Adverse Event Severity

Adverse events are graded by the investigator as Grade 1 (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" data listings.

7.1.3. Relationship of Adverse Events to Study Drug

Related AEs are those for which the investigator selected "Related" on the AE eCRF to the question of "Related to Study Treatment." Events for which the investigator did not record relationship to study drug will be considered related to study drug for summary purposes. However, by-subject data listings will show the relationship as missing.

7.1.4. Serious Adverse Events

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

7.1.5. Treatment-Emergent Adverse Events

7.1.5.1. Definition of Treatment-Emergent Adverse Events

Treatment-emergent adverse events (TEAEs) 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

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

7.1.5.2. Incomplete Dates

If the onset date of the AE is incomplete and the AE stop date is not prior to the first dosing date of randomized study drug, 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 for the randomized phase 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 randomized 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 the minimum of (1) the randomized phase last dose date plus 30 days AND (2) the extension phase first dose date minus 1 day

The event is considered treatment emergent for the extension phase if both of the following 2 criteria are met:

- The month and year (or year) of the AE onset is **after** the month and year (or year) of the first dosing date of extension phase 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 extension phase 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 randomized study drug, will be considered as a TEAE for the randomized phase. 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 the randomized study drug will be considered as a TEAE for the randomized phase.

7.1.6. Summaries of Adverse Events and Death

Only TEAEs in the randomized phase will be included in the summary tables. 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 reported in the randomized phase and 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 randomized phase will be also included in this summary.

Treatment-emergent death refers to deaths that occurred between the randomized phase first dose date and the randomized phase 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 TEAEs, Grade 3 or 4 TEAEs, treatment-emergent study drug-related AEs, Grade 2, 3, or 4 treatment-emergent study drug-related AEs, and treatment-emergent SAEs will be summarized by PT only, in descending order of total frequency.

In addition, data listings for all AEs regardless of the study phases will be provided for the following:

- All AEs
- Grade 3 and 4 AEs

- SAEs
- Study-Drug-Related SAEs
- Deaths report
- AEs leading to premature discontinuation of study drug

7.1.7. Additional Analysis of Adverse Events

7.1.7.1. Stage 3 Opportunistic Illnesses in HIV

On an ongoing basis, AEs will be reviewed for events that might meet the definition of stage 3 opportunistic illnesses in HIV that are indicative of an AIDS-defining diagnoses (see Protocol Appendix 5). The Gilead medical monitor will review the possible stage 3 opportunistic illnesses and approve the events that meet the definition. Events that meet the stage 3 opportunistic illness definition of an AIDS-defining diagnosis will be listed.

7.1.7.2. Cardiovascular or Cerebrovascular Events

Preferred terms for defining cardiovascular or cerebrovascular events are from relevant Standardised MedDRA Query (SMQ). The selected PT listing was provided by Gilead DSPH and reviewed by Gilead medical monitors, which is the same PT listing used to search "Cardiovascular Disease" medical history (see details in Appendix 3).

The number and percentage of subjects with treatment-emergent cardiovascular or cerebrovascular events and serious cardiovascular or cerebrovascular events by PT will be provided 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.

7.1.7.3. Hepatic Events

Preferred terms for defining hepatic events are from 15 relevant SMQs, which are identified as non-infectious and non-congenital hepatobiliary disorders. The selected PT listing was provided by Gilead DSPH and reviewed by Gilead medical monitors (see details in Appendix 4).

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 Fisher's exact test. A data listing of hepatic events will be provided.

7.2. Laboratory Evaluations

Laboratory data collected during the randomized phase of 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 for all data collected from both phases of the study. Values falling outside of the reference range and/or having a severity grade of 1 or higher on the Gilead Grading Scale for Severity of Adverse Events and Laboratory Abnormalities will be flagged in the data listings, as appropriate.

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 randomized 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 x (4.0 – albumin (g/dL)).

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

Estimate GFR

The following formulae 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.

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

For the international normalized ratio (INR) of prothrombin time (PT), protocol-specified toxicity grading scale depends on the upper limit of normal range (ULN). While the ULN of INR depends on whether the subject is taking anticoagulant medication or not (ie, Not taking oral anticoagulant: 0.8 – 1.2; Taking oral anticoagulant: 2.0 – 3.0), this information is not collected by the reference laboratory. As a result, INR will be graded by assuming subject is not taking an oral anticoagulant, which is a conservative approach that may lead to over-reporting of abnormalities for INR. Consequently, INR and PT will not be included in summaries of laboratory abnormalities, but will be included in listings for the following reasons: 1) INR and PT are reflexive tests; 2) only the absolute values, not the toxicity grade, are needed for subject management purposes; and 3) more importantly, the toxicity grades for INR may be over-reported.

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 from the randomized phase last dose date. 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 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 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 the randomized phase last dose 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 metabolite 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 the 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 randomized phase of 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 randomized phase of 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 collected in the randomized phase of this study:

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

The summary will include data from all postbaseline visits up to 30 days after the randomized phase last dose date. 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.

Furthermore, ALT flare, defined as subjects with ALT elevation > 2 x Baseline ALT and > 10 x ULN and confirmed at 2 consecutive visits, will be evaluated and listed for subjects with HIV/HBV coinfection at baseline.

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

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 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 randomized phase 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. 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 at 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 randomized study drug. Change from baseline to a postbaseline visit will be defined as the postbaseline value minus the baseline value.

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

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

7.4. Prior and Concomitant Medications

7.4.1. Antiretroviral Medications

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

7.4.2. Prior Antiretroviral Medications

Prior ARV medications are defined as ARV medications taken on or up to 2 days prior to the first dose date of randomized study drug based on ARVs reported on ARV eCRF (see Appendix 5 for details). The number and percentage of subjects in each prior ARV regimen will be summarized as part of baseline disease characteristics table.

7.4.3. Concomitant Non-Antiretroviral 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 the randomized phase first dose date to the randomized phase last dose date will be summarized

(number and percentage of subjects) by treatment group and preferred name. Multiple drug use (by preferred name) will be counted only once per subject. The summary will be sorted by decreasing order of total frequency.

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 for the randomized phase of the study. 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 randomized phase last dose date
- The month and year of stop of the medication is before the randomized phase first dose date

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

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.

7.5. 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.

7.6. Other Safety Measures

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

7.7. 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. In addition, subgroup analysis by prior treatment regimen (ie, TDF-containing regimen versus non-TDF containing regimen) will be performed for renal endpoints including urine RBP to creatinine ratio, beta-2 microglobulin to creatinine ratio, and UACR.

7.8. Changes From Protocol-Specified Safety Analyses

No change from protocol-specified safety analysis is planned.

8. PHARMACOKINETIC ANALYSES

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

The following listings will be provided for trough and postdose PK analysis for subjects in the PK analysis set:

- Listing of PK sampling details ("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 single PK, trough PK, and postdose PK samples will be included in one listing. Similarly, study drug administration records for single PK, trough PK, and postdose PK samples will also be included in one listing.

8.2. Changes from Protocol-Specified Pharmacokinetic Analysis

No change from protocol-specified PK analyses is planned.

9. SPECIAL POPULATION ANALYSES

Only randomized phase data will be included for the special population analyses.

9.1. Analyses for HIV/HBV Coinfected Subjects

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

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

The following analyses will be provided by treatment and overall for subjects with HIV/HBV coinfection at baseline:

- The proportion of subjects with HBV DNA < 29 IU/mL at baseline and Week 48
- Treatment-emergent adverse events overall summary
- Treatment-emergent adverse events by SOC, HLT, and PT
- Treatment-emergent laboratory abnormalities
- The change from baseline for liver-related laboratory tests, including ALT, AST, ALP, total bilirubin, direct and indirect bilirubin
- Listing of adverse events
- Listing of liver-related laboratory tests and HBV DNA results

HBV DNA will be analyzed using observed, on-treatment data (ie, data collected up to the 1 day after the randomized phase last dose date) for subject in the FAS with HIV/HBV coinfection at baseline.

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 randomized phase first dose date and on or prior to the randomized phase last dose date, or
- Negative HBsAg, negative HBsAb, positive HBcAb, and quantifiable HBV DNA (ie, HBV DNA ≥ 20 IU/mL) after the randomized phase first dose date and on or prior to the randomized phase last dose date, or

- Experience any of the following adverse events (ie, selected MedDRA PTs from the SMQ of "Liver Infections") after the randomized phase first dose date and on or prior to the randomized phase last dose date: 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 HCV antibody (HCVAb) and quantifiable HCV RNA (ie, HCV RNA ≥ 15 IU/mL) on or prior to the randomized phase first dose date. The following analyses will be conducted for subjects with HIV/HCV coinfection at baseline:

- Treatment-emergent adverse events overall summary
- Treatment-emergent adverse events by SOC, HLT, and PT
- Treatment-emergent laboratory abnormalities
- 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 randomized phase first dose date and on or prior to the randomized phase last dose date with baseline HCVAb Negative or missing, or
- Quantifiable HCV RNA (ie, HCV RNA ≥ 15 IU/mL) after the randomized phase first dose date and on or prior to the randomized phase last dose date, or
- Experience any of the following adverse events (ie, selected MedDRA PTs from the SMQ of "Liver Infections") after the randomized phase first dose date and on or prior to the randomized phase last dose date: 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.

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

11. SOFTWARE

SAS® Version 9.4 (SAS Institute Inc., Cary, NC, USA) 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 Table

Study Procedure	Screening[a]	Day 1[b]	End of Week[c]						Post Week 48[d,v]	30 Day Follow-Up[e]	ESDD[f]
			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
Adverse Events	X	X	X	X	X	X	X	X	X	X	X
Complete Physical Exam	X	X				X		X			X
Symptom-Directed Physical Exam			X	X	X		X		X	X	
12-Lead ECG	X	X				X		X			X
Height	X										
Weight	X	X	X	X	X	X	X	X	X	X	X
Vital Signs[g]	X	X	X	X	X	X	X	X	X	X	X
Urinalysis	X	X	X	X	X	X	X	X	X	X	X
Urine Chemistry[h]		X				X		X	X[w]		
Urine Pregnancy Test[i]		X	X	X	X	X	X	X	X	X	X
Serum Pregnancy Test[i]	X										
Chemistry Profile[j]	X	X	X	X	X	X	X	X	X	X	X
Metabolic Assessments[k]		X			X	X		X	X[w]		
Estimated GFR	X	X	X	X	X	X	X	X	X	X	X
Hematology Profile[l]	X	X	X	X	X	X	X	X	X	X	X
Plasma HIV-1 RNA[m]	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
HBV Blood Planel[n]	X										

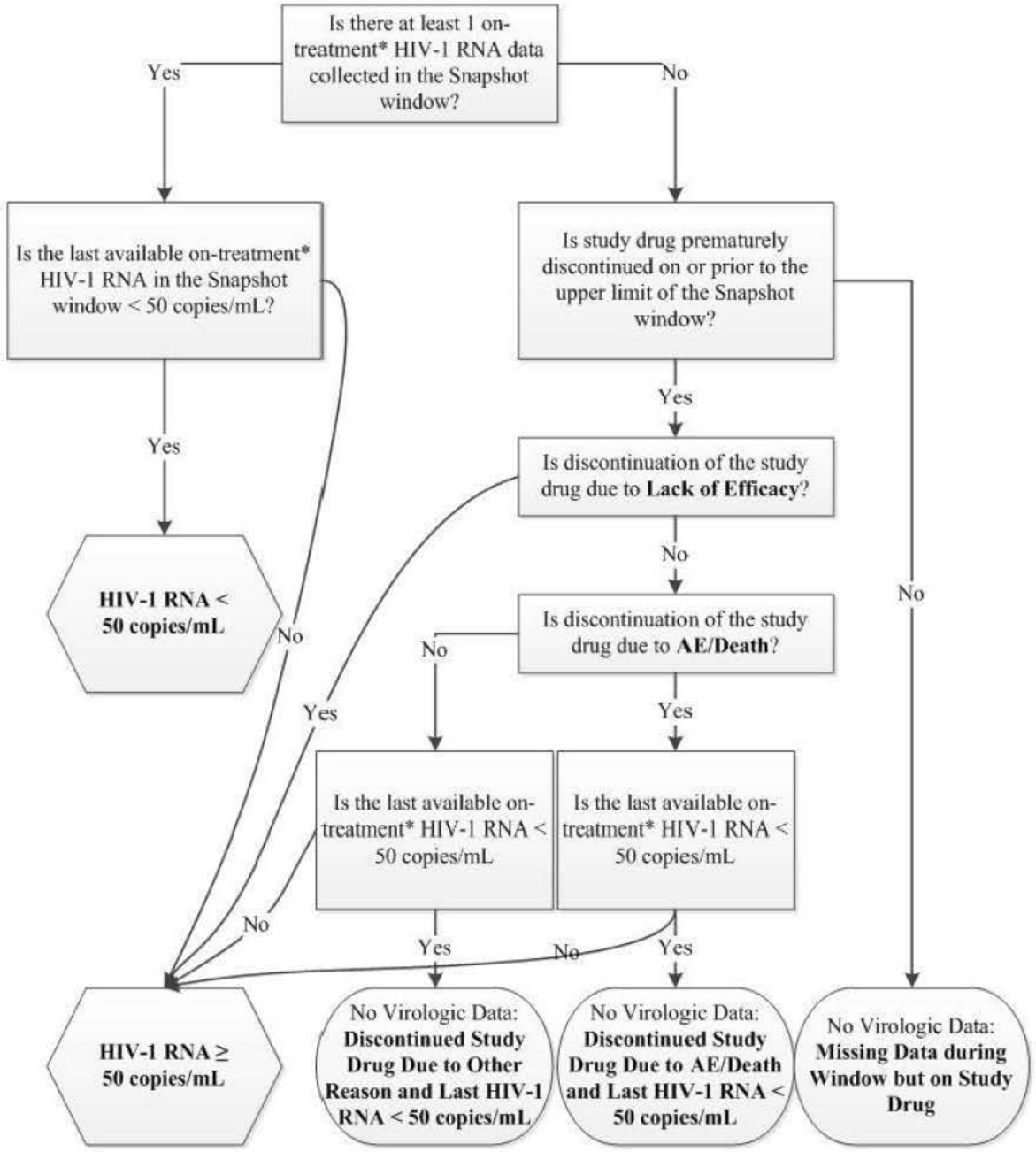
Study Procedure	Screening[a]	Day 1[b]	End of Week[c]						Post Week 48[d,v]	30 Day Follow-Up[e]	ESDD[f]
			4	8	12	24	36	48	Every 12 Weeks		
Plasma HBV DNA[o]		X			X	X		X	X[w]		X
HCVAb[p]	X										
HCV RNA[p]	X					X		X	X[w]		
HIV-1 Genotype/Phenotype[q]								X[q]			X[q]
Single PK Draw[r]				X		X	X				
Trough PK Draw[s]			X		X						
PK Sample (post-dose)[s]			X		X						
Observed In-Clinic Dose[s]			X		X						
Provide Dosing Diary[u]		X	X	X	X	X					
Collect Dosing Diary[x]			X	X	X	X	X				
Plasma Sample Storage[t]		X	X	X	X	X	X	X	X		X
Urine Sample Storage[t]		X	X	X	X	X	X	X	X		X
Whole Blood Storage Sample[t]		X									
PPD		X									
Randomization		X									
Study Drug Dispensation		X	X	X	X	X	X	X[v]	X[v]		
Study Drug Accountability			X	X	X	X	X	X	X		X

a Evaluations to be completed within 30 days prior to Day 1.
b Subjects should initiate dosing of study drug on the same day as the Day 1 visit.
c All study visits should be ± 2 days of the protocol-specified visit date based on the Day 1 visit through Week 12 and completed within ± 6 days at Week 24 and Week 36, unless otherwise specified. The visit window at Week 48 will be ± 6 weeks of the protocol-specified visit date.
d At the Week 48 Visit, 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 for an additional 48 weeks, or until the product becomes accessible to subjects through an access program, or until Gilead Sciences elects to discontinue the study in that country, whichever occurs first. Study visits are to be completed every 12 weeks, within ± 6 days of the protocol-specified visit date unless otherwise specified.

e Must be completed 30 days after discontinuing study drug. For the purpose of scheduling a 30-Day Follow-Up Visit, a ± 6 days window may be used. Required for subjects who permanently discontinue study drug prior to Week 48 and do not continue in the study through at least one subsequent visit after the ESDD visit. Subjects who participate post Week 48 will be required to return to the clinic 30 days after the completion of study drugs for the 30-Day Follow-Up Visit.
f Early Study Drug 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 Week 48 Visit even if the subject discontinues study drug.
g Vital signs measurements including blood pressure, pulse, respiratory rate, and temperature
h Urine Chemistry includes urine albumin, urine creatinine, urine protein, retinol binding protein, and beta-2 microglobulin
i Women of childbearing potential only. Positive urine pregnancy tests will be confirmed with a serum test.
j Chemistry profile: alkaline phosphatase, AST, ALT, GGT, total bilirubin, direct and indirect bilirubin, total protein, albumin, 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 24, and 48 and every 24 weeks during the post Week 48 period, analyses of glucose will be done as part of the fasting metabolic assessments and not as part of the chemistry profile. TSH will be collected at Screening, Day 1, Weeks 24, and 48, as well as every 24 weeks post Week 48, and ESDD if applicable.
k Fasting 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.
l CBC with differential and platelet count.
m If the HIV-1 RNA value is ≥ 50 copies/mL at Week 48, a retest HIV-1 RNA value must be collected within two to three weeks of the initial test.
n Hepatitis B Virus (HBV) blood panel: Hepatitis B virus surface antigen (HBsAg), Hepatitis B virus surface antibody (HBsAb) and Hepatitis B virus core antibody (HBcAb). If positive HBsAg, reflex testing for plasma HBV DNA, HBeAg (if negative, reflex HBeAb), and quantitative HBsAg. If positive HBcAb with negative HBsAg and negative HBsAb, reflex testing for plasma HBV DNA (if positive, reflex HBeAg). If HBeAg is performed and found to be negative, reflex HBeAb.
o For subjects who meet the definition of HBV infection, the following will be conducted by the central laboratory: HBsAb, HBsAg (qualitative and quantitative) and HBeAg (if negative, reflex HBeAb) at Days 1, 12, 24 and then every 24 weeks.
p Subjects who are HCVAb positive will have a HCV RNA test performed at screening and every 24 weeks.
q HIV-1 genotype/phenotype testing for subjects with HIV-1 RNA ≥ 200 copies/mL and virologic rebound, at early study drug discontinuation or Week 48. Following unconfirmed 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/phenotype (reverse transcriptase, protease and integrase) blood draw. Based on the results of this testing, subjects should be managed according to the Virologic Rebound Schema (Section 6.13.1).
r All subjects on GS-9883/F/TAF (Treatment Group 1 only) will have a single anytime PK blood sample collected at Weeks 8, 24 and 36.
s Subjects on GS-9883/F/TAF (Treatment Group 1 only) will have a Trough PK blood sample collected between 20-28 hours following their last dose at Weeks 4 and 12. Subjects must be instructed to not take their study drugs on the morning of their visit for the trough sample collection. If the subject has taken their dose of study drugs prior to the visit, the visit may proceed, but the subject must return within 72 hours for the single trough PK blood sample collection. In the event a subject routinely takes their study drug in the evening, a single anytime sample may be drawn at Weeks 4 and 12 as the subject will not be instructed to change their dosing time to accommodate this trough PK draw. A post-dose PK blood sample will be collected between 1 and 4 hours post dose following an observed, in-clinic dose.
t Plasma storage samples banked for possible future protocol-related testing (safety, virology, pharmacokinetic analysis). Urine storage samples banked for possible future protocol-related safety testing including urine chemistry. Whole blood sample for potential virologic resistance testing and/or HIV DNA genotyping. PPD
u A dosing diary will be dispensed for all Treatment Group 1 subjects to complete prior to each of the PK sample visits.
v Open-label GS-9883/F/TAF FDC will be dispensed to subjects participating in the study post Week 48 starting at the Week 48 Visit.
w Every 24 weeks only.
x Dosing diaries will be collected from subjects for the single anytime PK and trough PK collection (Treatment Group 1 only). If a dosing diary is not returned the site may ask the subject for the time of the last dose and if it was taken with or without food.

Appendix 2. Flowchart of US FDA-defined Snapshot Algorithm

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. 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 following selected PT listing for the corresponding disease with start date on or prior to the randomized phase first dose date.
- At least 1 AE record with MedDRA PT (ae.MDRPT) in the following selected PT listing for the corresponding disease with start date on or prior to the randomized phase first dose date.
- At least 1 concomitant medications record with medication class and indication in the following selected listing for the corresponding disease with start date on or prior to the randomized phase first dose date.

If the start date is incomplete but the month and year (or year alone) of the start date is the same as or before the month and year (or year alone) of the first dosing date of randomized study drug, the event will be included. If the start date is completely 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 AE record will be flagged for a disease of interest if its MedDRA PT included in the following 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, two variables (ie, DRUGF and DRUGTYP) 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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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
165	CALCIUM CHANNEL BLOCKERS	SECONDARY STROKE PREVENTION	AMLODIPINE
166	CALCIUM CHANNEL BLOCKERS	SICK SINUS SYNDROME	VERAPAMIL

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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
48	LIPID MODIFYING AGENTS	HYPERCHOLESTERINAEMIA	ATORVASTATIN
49	LIPID MODIFYING AGENTS	HYPERCHOLESTERINAEMIA	PRAVASTATIN
50	LIPID MODIFYING AGENTS	HYPERCHOLESTERINEMIA	PRAVASTATIN
51	LIPID MODIFYING AGENTS	HYPERCHOLESTERINEMIA	SIMVASTATIN

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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

	Medication Class (WHOATC2)	Indication (CMINDC)	WHOGEN
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
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 4. Hepatic Events

An adverse event record will be flagged as a hepatic event if its MedDRA PT included in the 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 5. 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 (randomized phase 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 randomized phase Day 1 have the month in common and the birthday is later in the month than the date of randomized phase Study Day 1, then subtract one from the AGE result above.

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

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

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

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

5. 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 randomized 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. Only 1 study completion form is collected for the entire study. Therefore, study disposition in the randomized phase of the study is defined as follows for subjects who were dosed with randomized study drug:

a) Subjects who completed study in the randomized phase include the following two exclusive cases:

   i) Subjects who were dosed in the extension phase (ie, extension phase first dose date is present), OR

   ii) Subjects who were not dosed in the extension phase and completed study (ie, extension phase first dose date is not present and study completion form is marked as "Yes")

b) Subjects who are ongoing in the randomized phase of the study include subjects who were not dosed in the extension phase of the study, and study completion form was not filled.

c) Subjects who discontinued study in the randomized phase of the study include subjects who were not dosed in the extension phase of the study and study completion form was marked as "No".

8. Body mass index (BMI) and Body Surface Area (BSA)

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

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

   Baseline height and weight in the randomized phase of the study will be used for this calculation.

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

   1) 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;
```

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

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

   3) 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;
```

Note: "Not Permitted", "Unknown", or missing categories will be excluded for percentage calculation and also be excluded for p-value generation for categorical data analysis (eg, CMH test or Fisher exact test), except for Mode of Infection (HIV Risk Factors), where "Unknown" will be included for percentage calculation since a subject may fit more than 1 HIV risk factors. For this variable, percentage may add up to be more than 100% and no p-value will be generated.

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

10. SAS code for the 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); /*0 indicates censored observation*/
       Strata TRT01AN;
       label TRTDURD = "Duration of Exposure (Days)";
run;
```

11. Last Dose Date and Last Study Date

    1) Last Dose Date (ie, TR01EDTC and TR01EDT for randomized phase last dose date, and TR02EDTC and TR02EDT for extension phase last dose date) in ADSL was defined in Section 3.8.1.

       Randomized Phase Last Dose Date:

       For subjects with a partial last dosing date (ie, month and year of last dose are known), the minimum of {(death date, if available), (extension phase first dose date – 1 day, if available), (the latest of the dispensing dates of study drug bottles, study drug start dates and end dates (based on EX dataset), 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.

       Please note the follows:

       - Last dose date is not defined for subjects still on randomized study drug. However, for the calculation of the duration of exposure to randomized study drug, the data cut date will be used to impute the last dose date for subjects who have not discontinued study drug by the data cut date. For Week 48 interim analysis, 22 Sep 2017 will be the data cut date for subjects with Week 48 visit on or prior to 22 Sep 2017, subjects missing Week 48 visits while on study drug, or subjects who permanently discontinued the

randomized study drug. For subjects with Week 48 visit after 22 Sep 2017, the last subject's Week 48 visit date will be used as the data cut date.

- For time to premature discontinuation of study drug KM summary, if we have subjects with duration of exposure of study drug great than 378 days (ie, upper limit of the Week 48 visit window), please add Week 60, defined as Day 379 – Day 462 (inclusive), to the table.

Extension Phase Last Dose Date:

For subjects with a partial last dosing date (ie, month and year of last dose are known), the minimum of {(death date, if available), (the latest of the dispensing dates of study drug bottles, study drug start dates and end dates (based on EX dataset), 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.

Last dose date is not defined for subjects still on study drug in SAP. However, for programing purposes, the data cut date will be used to impute the last dose date for subjects still on study drug.

2) 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 dates or end dates is partially missing (ie, only year and month are known), the day will be imputed as 15 for the purpose of this analysis.

   Last study date is not defined for subjects still on study in SAP. However, for programing purpose, the latest of data cut date, 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:

1) For toxicity grade summaries, include all postbaseline graded results up to 30 days after the randomized phase last dose of study drug, not just those used in by-visit summaries.

2) 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:

1) 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 2 treatment groups and its 95.001% CIs (or 95% CI for M=F and M=E analyses) are calculated based on the an unconditional exact method with 2 inverted 1-sided tests in SAS v9.3 or above. Please see example SAS codes below:

```
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=0.04999;
weight count; exact RISKDIFF(METHOD=SCORE);
output out=ciexact(keep=_RDIF1_ XL_RDIF1 XU_RDIF1) riskdiff;
run;

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;
```

2) Homogeneity test: Homogeneity Test of Treatment Effect across country in HIV-1 RNA < 50 copies/mL at Week 48 (Snapshot Algorithm). For each country, 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 country and treatment group as follows.

```
proc freq data=xxx;
   tables country*treat*Y/all; /*p value from Breslow Day test*/
run;
```

3) Homogeneity test: Homogeneity Test of Treatment Effect between Subgroups in HIV-1 RNA < 50 copies/mL at Week 48 (Snapshot Algorithm)

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

```
proc genmod data=data descending;
   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: 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.

4) 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 effects in the model.

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

5) 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:

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

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

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

   d. 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.

6) Snapshot definition clarification:

   a. For a subject who completed the randomized phase study with Week 48 HIV-1 RNA missing for the randomized phase of the study, snapshot outcome for such subject would be "Missing data during the window but on study drug".

14. Clarification of the LOCF algorithms for CD4: (1) baseline value will be carried forward; (2) 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.

15. Graded Laboratory Abnormalities Summary

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

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

Battery	Lab Test Label Used in l-labtox Listing	Toxicity Direction	Lab Test Label Used in t-labtox Table
	Uric Acid	Decrease	Uric Acid (Hypouricemia)
	Prothrombin Intl. Normalized Ratio (INR)	Increase	N/A
	Prothrombin Time (PT)	Increase	N/A
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)

Note: Prothrombin Intl. Normalized Ratio (INR) and Prothrombin Time (PT) were graded based on the protocol defined toxicity grade scale. The results and toxicity grade will be listed in listing, but not be summarized in lab toxicity summary table.

16. Renal related laboratory evaluation

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

        a) Urine RBP (ug/L) to creatinine (mg/dL) ratio: 1 (ug/L) / (mg/dL) = 100 x ug/g

        b) Urine Beta-2-microglobulin (mg/L) to creatinine (mg/dL) ratio: 1 (mg/L) / (mg/dL) = 10^5 ug/g

        c) Urine Albumin (mg/dL) to creatinine (mg/dL) ratio: 1 (mg/dL) / (mg/dL) = 1000 x mg/g

    2) Calculation of ratios:

        To calculate laboratory ratios (eg, urine RBP to creatinine ratio), the 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 , then the ratio is not calculable (ie, missing).

17. Smoking history at baseline

    Smoking history at baseline (ie, never smoker, former smoker, and current smoker) will be summarized as part of the baseline disease characteristics. How to classify a subject as never, former, or current smoker 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, 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"; the subject will be flagged as a "Former" smoker, if all selected records have a flag of "Prior" or a combination of "Prior" and "Post"; Otherwise, the subject will be flagged as a "Current" smoker.

	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 History	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 missing (ie, at least year is known) or the start date is not missing and record is ongoing. The completed 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 before (≤) 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) 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 and should be queried first. However, this record is flagged as "Present" if the start date is on the first dose date; this record is flagged as "Post" if the start date is after the first dose date.

Note: first dose date for smoking history definition at baseline refers to the randomized phase first dose date.

18. 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).

19. Non-study drug ARV medications (ie, ARV medications other than study drug that are taken while receiving study drug) will be flagged in "Antiviral Medication" listing. Please note that for ARVs recorded on the "Prior ARV" eCRF will NOT be considered as ARVs taken during study. All Prior ARVs with missing end date will be queried to confirm the ARVs were stopped before the randomized phase 1st dose date.

20. 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 use of the lipid modifying agents at study day 1 (ie, the randomized phase first dose date). More specifically, subjects with "Lipid Modifying Agent Use at Study Entry" include those subjects in safety analysis set with: 1) any selected CM record with the start date ≤ the randomized phase first dose date, and 2) the end date of the selected CM record is ongoing or the end date of the selected CM record ≥ the randomized phase first dose date.

- Subjects who initiated lipid modifying medications during the randomized phase study include the following subjects in the safety analysis set: (1) for subjects who permanently discontinued randomized phase study drug with any selected CM record started after the randomized phase first dose date and on and prior to the minimum of randomized phase last dose date and (extension phase first dose date minus 1 day); (2) for subjects who are still on randomized study drug (if applicable) with any selected CM records started after the randomized phase first dose date; (3) lastly, for subjects who meet criteria (1) or (2) above, if they took lipid modification medications at study entry, they will be NOT be considered taking lipid modifications during the randomized phase study.

- For lipid modifying medications with start date completely unknown, we assume the start date is on or before the randomized phase 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).

- Lipid modifying medications with the start date on or prior to the randomized phase first dose date and the end date completely unknown were considered as being taken at study entry.

21. 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.

22. Prior ARV regimen

    All subjects will have one of the following prior ARV regimen identified based on ARVs entered in the ARV eCRF: E/C/F/TAF, E/C/F/TDF, ATV+RTV+FTC/TDF.

    Use ARV dataset and include all prior and/or current ARVs (ARV.CMSCAT = 'Prior ARV' or 'Current ARV') with taken on or up to 2 days prior to the randomized phase first dose date meeting the following criteria:

If CMTRT contains Only the specified ARVs:	**Re-code as follows for baseline regimen**
E/C/F/TAF	E/C/F/TAF
GENVOYA	
NRTI/INI: GENVOYA (EVG+COBI+FTC+TAF)	
EVG/COBI/FTC/TDF	E/C/F/TDF
NRTI/INI: STRIBILD (EVG+COBI+FTC+TDF)	
ATAZANAVIR/RITONAVIR+FTC+TDF	ATV+RTV+FTC/TDF
ATV/R+FTC/TDF	
NRTI: TRUVADA (FTC+TDF) or PI: ATAZANAVIR (ATV) or PI: RITONAVIR (RTV)	
TDF/FTC/ATV/R	

23. 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 when < 29 IU/mL, NUMERICAL VALUE when ≥ 29 IU/nL* *
HCVAb	CNT350	Hepatitis C Virus Antibody	"Positive"*, "Indeterminate", "Negative"
HCVAb	CNT458	Hepatitis C AntibodyEDTApl-CL	"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

HBsAg	HBsAb	HBcAb	HBV DNA	Coinfection Status
		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

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

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

24. 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", 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. If reflexive test is not available, HBV DNA level will be determined based on lab test code GET1883.

25. Puerto Rico was combined with the United States when we evaluate the treatment effect across countries.

26. LDL: Conversions between 2nd and 3rd generations

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

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

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

    For this analysis, since most of the LDL tests were from the 2nd generation, we only requested conversion from 3rd generation to 2nd generation.

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

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

27. AE action taken for study drug regimen containing multiple pills (eg, ATV + RTV + FTC/TDF) is derived as the most severe actions from all pills in the regimen. The increasing order of severity of AE action taken is: Unknown, Not Applicable, Dose Not Changed, Drug Interrupted, and Drug Withdrawn.