STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 4 Study to Evaluate the Safety, Pharmacokinetics and Efficacy of Oral B/F/TAF after Discontinuing Injectable CAB + RPV
Name of Test Drug:	B/F/TAF
Study Number:	GS-US-380-6738
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LIST OF ABBREVIATIONS

ADA	antidrug antibody
AE	adverse event
ALT	alanine aminotransferase
ART	antiretroviral therapy
ARV	antiretroviral
AST	aspartate aminotransferase
B/F/TAF	bictegravir/emtricitabine/tenofovir alafenamide (coformulated; Biktarvy®)
BIC, B	bictegravir
BVY	Biktarvy®
BLQ	below the limit of quantitation
BMI	body mass index
CAB	cabotegravir
CBC	complete blood count
CD4	clusters of differentiation 4
CI	confidence interval
CK	creatine kinase
CRF	case report form
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
DAIDS	Division of AIDS
DMC	data monitoring committee
ECG	electrocardiogram
eCRF	electronic case report form(s)
EDC	electronic data capture
eGFR	estimated glomerular filtration rate
ESDD	early study drug discontinuation
ESRD	end-stage renal disease
ET	early termination
EU	European Union
FAS	Full Analysis Set
FDA	Food and Drug Administration
FDC	fixed-dose combination
FTC, F	emtricitabine (Emtriva®)
Gilead	Gilead Sciences/Gilead Sciences, Inc.
Hb	hemoglobin
HBcAb	hepatitis B core antibody
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus

HCV	hepatitis C virus
HDL	high-density lipoprotein
HIV, HIV-1	human immunodeficiency virus type 1
HIVTSQc	HIV Treatment Satisfaction Questionnaire Change
HIVTSQs	HIV Treatment Satisfaction Questionnaire Status
HLT	high-level term
INSTI	integrase strand-transfer inhibitor
IRB	institutional review board
LDL	low-density lipoprotein
LLT	lowest-level term
LOQ	limit of quantitation
MedDRA	Medical Dictionary for Regulatory Activities
NNRTI	nonnucleoside reverse transcriptase inhibitor
NRTI	nucleoside reverse transcriptase inhibitor
NtRTI	nucleotide reverse transcriptase inhibitor
OL	open-label
PK	pharmacokinetic(s)
PP	per protocol
PT	preferred term
Q1, Q3	first quartile, third quartile
Q2M	Twice monthly
QRS	electrocardiographic deflection between the beginning of the Q wave and termination of the S wave representing time for ventricular depolarization
RPV	Rilpivirine
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SI (units)	international system of units
SOC	system organ class
SOP	standard operating procedure
TAF	tenofovir alafenamide (Vemlidy®)
TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
TFV	Tenofovir
TFV-DP	tenofovir diphosphate
ULN	upper limit of normal
US	United States
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 final analysis for Study GS-US-380-6738. This SAP is based on the study protocol dated 27 July 2023 and the electronic case report form (eCRF). The SAP will be finalized prior to database finalization.

1.1. Study Objectives and Endpoints

Primary Objective	Co-primary Endpoints
• To assess the safety of switching to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in virologically suppressed participants unable/unwilling to continue on cabotegravir and rilpivirine (CAB+RPV) IM injections or wishing to switch to oral therapy through Week 12	• Proportion of participants experiencing treatment-emergent Grade 3 or 4 study drug-related adverse events (AEs) through Week 12 • Proportion of participants experiencing treatment-emergent Grade 3 or 4 laboratory abnormalities through Week 12
Secondary Objectives	**Secondary Endpoints**
• To assess the pharmacokinetics of bictegravir (BIC), CAB and RPV after switching to B/F/TAF from CAB+RPV • To assess the efficacy and persistence of B/F/TAF after switching from CAB+RPV • To assess the safety of B/F/TAF after switching from CAB+RPV through Week 24 • To evaluate treatment satisfaction of switching to B/F/TAF from CAB+RPV	• Plasma concentrations of BIC, CAB and RPV at Day 1, Week 4, 12, and 24, as appropriate • Proportion of participants with HIV-1 RNA ≥ 50 copies/mL at Weeks 12 and 24 (missing = excluded and discontinuation = failure) • Number and proportion of participants with B/F/TAF discontinuation by Weeks 12 and 24 • Proportion of participants experiencing treatment-emergent grade 3 or 4 laboratory abnormalities through Week 24 • Change in HIV treatment satisfaction (HIVTSQc) score at Week 4
Exploratory Objectives	**Exploratory Endpoints**
• To understand PWH experience with injectable and oral therapies for HIV treatment • To evaluate reasons for switching to B/F/TAF from CAB+RPV	• Participant reported experiences with CAB+RPV, preferences for injectable and oral therapies • Participant reported reasons for switching to B/F/TAF

1.2. Study Design

1.2.1. Study Design Overview

This study was a Phase 4, single-arm, open-label, multicenter interventional switch study to evaluate the safety, pharmacokinetic (PK), and efficacy of daily oral bictegravir 50 mg/emtricitabine 200 mg/tenofovir alafenamide 25 mg (B/F/TAF) fixed-dose combination (FDC) in virologically-suppressed participants ≥ 18 years who were unable/unwilling to continue on cabotegravir and rilpivirine (CAB+RPV) IM injections or wishing to switch to oral therapy.

A total of approximately 35 participants (with at least 20 participants in North America with evaluable PK) were anticipated to be enrolled in the study including approximately 10 participants in France. Participants in North America had safety, efficacy, and sparse PK assessments, received quantitative questionnaires, and were eligible for qualitative interviews, while participants in France had safety and efficacy assessments and received quantitative questionnaires.

After Screening procedures, study visits occurred at Day 1, and Weeks 4, 12 and 24. Laboratory analyses (chemistry, hematology, and urinalysis), HIV-1 RNA, assessment of AEs and concomitant medications, and complete or symptom directed physical examinations were performed at all study visits. Clusters of differentiation (CD4+) cell count were assessed at visits at Day 1 and Weeks 12 and 24. Adverse events and concomitant medications were assessed at each visit.

The laboratory analyses were performed at a central laboratory. Blood and urine samples for clinical laboratory assessments were collected as specified in the Study Procedures (see Schedule of Assessments, Appendix 1). Participants only needed to be fasted on days where lipid or fasting glucose profiling is scheduled. Fasting was defined as 8 hours without food or drink (except water) prior to laboratory draw.

A single PK plasma sample was collected at Day 1 prior to dose. A single trough plasma PK sample approximately 23 to 24 hours after the previous B/F/TAF dose and prior to B/F/TAF dosing on Weeks 4, 12, and 24, and a single plasma PK sample at approximately 2 hours post B/F/TAF dose, witnessed by study staff, at Weeks 4, 12, and 24 were to be collected.

Patient questionnaires and qualitative interviews were performed (see Schedule of Assessments, Appendix 1). HIV Treatment Satisfaction Status (HIVTSQs) were to be completed by the participant at Day 1 and Weeks 12 and 24. HIV Treatment Satisfaction Change (HIVTSQc) were to be completed by the participant at Week 4. Among the participants who were recruited and consented to undergo qualitative interviews, a vendor scheduled 1:1 interview with these participants over video communication platform. The qualitative interview occurred near the week 4 visit (visit widow range Week 3-9).

1.2.2. Duration of Intervention

Participants who met eligibility requirements were planned to be treated for 24 weeks.

After the participant completed/terminated their participation in the study, long-term care for the participant remained the responsibility of their primary treating physician.

1.2.3. Protocol-Specific Discontinuation Criteria

1.2.3.1. Criteria for Early Discontinuation for the Individual Participant

1.2.3.1.1. Criteria for Early Discontinuation for the Individual Participant from Study Intervention

Study drug was to be discontinued in the following instances:

- An adverse event (AE) that would, in the judgment of the investigator, affect assessments of clinical status to a significant degree. Following resolution of the AE, the participant might resume study dosing at the discretion of the investigator.
- Unacceptable toxicity, as defined in the Protocol Section 7.7, or toxicity that, in the judgment of the investigator, compromised the ability to continue study-specific procedures or was considered not to be in the participant's best interest.
- Lack of efficacy
- Participant requested to discontinue for any reason.
- Participant noncompliance. Participants who were noncompliant on an ongoing basis were be considered for discontinuation per the investigator's discretion or local treatment guidelines. Investigators who opted to discontinue study drug for an individual participant must discuss with the medical monitor prior to study drug discontinuation.
- Loss to follow-up.
- Discontinuation of the study by the sponsor.

1.2.3.1.2. Criteria for Early Discontinuation for the Individual Participant from the Study

The participant was discontinued from the study early in the following instances:

- Withdrawal of consent.
- Death.

1.2.3.2. Criteria for Early Discontinuation of the Study

The study was to be discontinued in the following instances:

- Discontinuation of the study at the request of Gilead, a regulatory agency, or an institutional review board/independent ethics committee (IRB/IEC).

1.2.3.3. Loss to Follow-up

Should the participant fail to attend a scheduled protocol-specified visit (eg, in-person, telephone, or virtual), sites needed to make at least 3 attempts by a combination of telephone and mail (electronic or physical) to contact the participant. Sites should document all attempts to contact the participant. If a participant did not respond within 5 days after the third contact, the participant was considered lost to follow-up and no additional contact will be required.

1.3. Sample Size and Power

The sample size in this study was determined based on practical considerations and past experience with similar types of studies. No sample size calculation was performed. A total sample size of approximately 35 participants (to obtain at least 20 participants with evaluable PK) should provide a suitable assessment of the descriptive PK and safety profile.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analysis

An interim analysis was conducted with plans for submitting the analysis to conferences/journals for presentation/publication purposes.

2.1.1. Week 12 Interim Analysis

There was 1 planned interim analysis after all participants at Northern American (NA) Sites had completed their Week 12 visit or prematurely discontinued the study drug. Only participants enrolled at NA sites were included in this interim analysis.

2.2. Final Analysis (Primary Analysis)

The final analysis will be performed after all participants have completed the study or prematurely discontinued from the study, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized. The analysis of the primary endpoints for all enrolled participants will be conducted at the time of the final analysis. This analysis will include all data collected during the study.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

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

By-participant listings will be presented for all participants in the All Enrolled Analysis Set and sorted by participant ID number in ascending order, visit date, and time (if applicable), unless otherwise specified. Data collected on log forms, such as AEs, will be presented in chronological order within the participant. Age, sex at birth, race, and ethnicity will be included in the listings, as space permits.

3.1. Analysis Sets

Analysis sets define the participants to be included in an analysis. Analysis sets and their definitions are provided in this section. The analysis set will be identified and included as a subtitle of each table, figure, and listing.

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

A listing of reasons for exclusion from analysis sets will be provided by participant.

3.1.1. All Enrolled Analysis Set

The All Enrolled Analysis Set includes all participants enrolled into the study after screening. This is the primary analysis set for listings.

3.1.2. Full Analysis Set

The Full Analysis Set (FAS) will include all enrolled participants who have received at least 1 dose of the study drug (B/F/TAF). This is the primary analysis set for analysis on efficacy and the participant reported outcomes (PROs).

3.1.3. Safety Analysis Set

The primary analysis set for safety analyses is defined as the Safety Analysis Set, which will include all enrolled participants who have received at least 1 dose of the study drug (B/F/TAF). All the data collected up to 30 days after participants permanently discontinue their study drug will be included in the safety summaries, unless specified otherwise.

3.1.4. Pharmacokinetic Analysis Sets

The primary PK analysis will be conducted on the following analysis sets. Only participants in North America will have sparse PK assessments.

- BIC PK Analysis Set will include all enrolled participants who have received at least 1 dose of study drug and have at least 1 nonmissing BIC concentration value reported by the PK laboratory test.

- CAB PK Analysis Set will include all enrolled participants who have received at least 1 dose of study drug and have at least 1 nonmissing CAB concentration value reported by the PK laboratory test.

- RPV PK Analysis Set will include all enrolled participants who have received at least 1 dose of study drug and have at least 1 nonmissing RPV concentration value reported by the PK laboratory test.

3.1.5. Participant Grouping

Summaries and analyses will be presented for one participant group: B/F/TAF.

3.2. Strata and Covariates

This study does not use a stratified randomization schedule when enrolling participants.
No covariates will be included in efficacy and safety analyses.

3.3. Examination of Participant Subgroups

Participants in North America (including USA and Canada) will have safety, efficacy, and sparse PK assessments, receive quantitative questionnaires, and be eligible for qualitative interviews, while participants in France will have safety and efficacy assessments and receive quantitative questionnaires. Since French participants did not undergo PK analysis, a subgroup analysis will be conducted on the demographic and baseline characteristics tables, to distinguish participants from North America sites vs. French sites. The groupings used in the final analysis are listed below.

Summary tables to be grouped by North America, France, and Total:

- Enrollment by country

- Participant disposition

- Important protocol deviation

- Demographics and baseline characteristics

- Duration of exposure to study drug (B/F/TAF)

- Adherence to study drug (B/F/TAF)
- Analysis sets
- Persistence with study drug (B/F/TAF)
- Post study antiretroviral medications.

Summary tables and figures to include participants from North America site only:

- Plasma BIC/CAB/RPV Concentrations.

Summary tables and/or figures to include participants from all sites as a Total group:

- HIV-1 RNA < 50 and >= 50 copies/mL for D = F and M = E approach
- CD4 cell count and CD4 percentage
- Adverse events and deaths
- Laboratory evaluations: hematology, chemistry, metabolic assessment, and laboratory abnormalities
- Vital signs
- HIV Treatment Satisfaction Status (HIVTSQs) and HIV Treatment Satisfaction Change (HIVTSQc)
- Study-specific questionnaire on Day 1: questions related to participant experience with CAB + RPV
- Study-specific questionnaire on Week 4: questions related to participant experience after switching to oral B/F/TAF.

All available data for participants from North America (USA and Canada) and France will be included in the data listings.

3.4. Multiple Comparisons

Adjustments for multiplicity will not be made, because no formal statistical testing will be performed in this study.

3.5. Missing Data and Outliers

3.5.1. Missing Data

Missing data can have an impact upon the interpretation of the trial data. In general, missing data will not be imputed unless methods for handling missing data are specified as follows.

- A missing pre-treatment laboratory result would be treated as normal (ie, no toxicity grade) for the laboratory abnormality summary.
- For missing last dosing date of study drug, imputation rules are described in Section 4.2. The handling of missing or incomplete dates for AE start is described in Section 7.2.6.2, and for prior and concomitant medications in Section 7.5.
- Missing PK sampling dates may be imputed based on other visit information. Missing PK sampling times may be imputed to nominal times. Missing drug concentrations will not be imputed.
- All available data for participants who do not complete the study will be included in the data listings.

3.5.2. Outliers

Outliers of non-PK data will be identified during the data management and data analysis process, but no sensitivity analyses will be conducted. All data will be included in the data analysis.

Outliers of PK data may be identified during review of data by the PK scientist, and if necessary, appropriate sensitivity analyses may be conducted.

3.6. Data Handling Conventions and Transformations

3.6.1. Data Handling Conventions and Transformations for Non-PK Data

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

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

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

If a partial date for medication/ART is recorded in the eCRF, the following convention will be used to assign the medication:

- If the partial date is a start date, a '01' will be used for missing days and 'Jan' will be used for missing months. For medications recorded separately in the eCRF as 'Current ARV', the latest of this imputed date or the first day of the IP (Investigational product) start will be used.

- if the partial date is a stop date, last day of the month will be used for the missing day and 'Dec' will be used for the missing month. For medications recorded separately in the eCRF as 'Prior ARV', the earlier of this imputed date or the day before the IP (Investigational product) start will be used.

HIV-1 RNA results of "No HIV-1 RNA detected" and "< 20 copies/mL HIV-1 RNA Detected" will be imputed as 19 copies/mL for analysis purposes.

HCV RNA results of "No HCV RNA detected" and "<15 IU/mL HCV RNA Detected" will be imputed as 14 IU/mL for analysis purposes.

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

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

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

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

3.6.2. Data Handling Conventions and Transformations for PK Data

Natural logarithm transformation will be used for analyzing non-BLQ concentrations and PK parameters in intensive PK samples as applicable. Concentration values that are BLQ will be presented as "BLQ" in the concentration data listing.

Values that are BLQ will be treated as 0 at predose and postdose time points for summary purposes. The number of samples will be summarized to reflect the actual number of samples assessed at that time point.

At predose, if all concentration values are BLQ, then the mean, and order statistics (minimum, Q1, median, Q3, and maximum) will be displayed as 0 and the rest of the summary statistics (ie, SD and CV) will be missing. If any values are non-BLQ, then the number of samples, order statistics, and all summary statistics will be displayed.

At any given postdose time point, if more than one-third of the participants have a concentration value of BLQ or less than 5 participants presented at the timepoint, then only the number of samples and order statistics will be displayed; otherwise, order statistics and summary statistics will be displayed.

The following conventions will be used for the presentation of order statistics for postdose time points in the summary tables:

- If at least 1 participant has a concentration value of BLQ for the time point, the minimum value will be displayed as "BLQ."
- If more than 25% of the participants have a concentration data value of BLQ for a given time point, the minimum and Q1 values will be displayed as "BLQ."
- If more than 50% of the participants have a concentration data value of BLQ for a given time point, the minimum, Q1, and median values will be displayed as "BLQ."
- If more than 75% of the participants have a concentration data value of BLQ for a given time point, the minimum, Q1, median, and Q3 values will be displayed as "BLQ."
- If all participants have concentration data values of BLQ for a given time point, all order statistics (minimum, Q1, median, Q3, and maximum) will be displayed as "BLQ."

Similarly, for PK concentration plotting, if more than one-third of the participants have a concentration values of BLQ or less than 5 participants presented at the timepoint, then the mean and standard deviation are not displayed at that timepoint; and if more than one-half of the participants have PK concentration values of BLQ or less than 5 participants presented at the timepoint, then the median and quartiles are not displayed at that timepoint.

3.7. Analysis Visit Windows

3.7.1. Definition of Study Day

Study Day 1 is defined as the day when the first dose of study drug (ie, B/F/TAF) was taken, as recorded on the Study Drug Administration eCRF. Study Day will be calculated from the first dosing date of study drug and derived as follows:

- For postdose study days: Assessment Date – First Dosing Date + 1
- For days prior to the first dose: Assessment Date – First Dosing Date

Last Dose Date is the latest of the study drug (B/F/TAF) end dates recorded on the Study Drug Administration eCRF form, with "Permanently Withdrawn" box checked for participants who prematurely discontinued or completed study drug according to the Study Drug Completion eCRF form.

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

Last Study Date is the latest non-missing study drug start/end date, clinic visit date, and the laboratory visit date, including the post-treatment follow-up visit date (if applicable) for participants who prematurely discontinued study or who completed study according to Study Completion eCRF form.

3.7.2. Analysis Visit Windows

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

The analysis windows for Plasma HIV-1 RNA, Hematology, Chemistry, Urinalysis and Urine Pregnancy Laboratory Tests, Vital Signs and Weight are provided in Table 3-1.

The analysis windows for CD4+ cell count, CD4 %, estimated GFR_{CG} (Estimated GFR according to the Cockcroft-Gault formula for creatinine Clearance), and Metabolic Assessments (including fasting glucose and lipid panel: total cholesterol, high density lipoprotein [HDL], direct low density lipoprotein [LDL], triglycerides, and total cholesterol to HDL ratio) are provided in Table 3-2.

Analysis windows for the HIVTSQs are provided in Table 3-3.

HIVTSQc and Qualitative Interviews (English only) are to be completed by the participant at Week 4 with analysis window shown in Table 3-4.

A study-specific questionnaire will be completed by the participant on Day 1 (Baseline) and Week 4 with analysis window shown in Table 3-5.

Table 3-1. Analysis Visit Windows for Plasma HIV-1 RNA, Hematology, Chemistry, Urinalysis and Urine Pregnancy Laboratory Tests, Vital Signs and Weight

Visit	Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Baseline	1	(none)	1
Week 4	28	2	56
Week 12	84	57	126
Week 24	168	127	210

Table 3-2. Analysis Visit Windows for CD4+ Cell Count, CD4 %, $eGFR_{CG}$, and Metabolic Assessments

Visit	Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Baseline	1	(none)	1
Week 12	84	2	126
Week 24	168	127	210

Table 3-3. Analysis Visit Windows for HIVTSQs

Visit	Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Baseline	1	(none)	1
Week 12	84	2	126
Week 24	168	127	210

Table 3-4. Analysis Visit Windows for HIVTSQc and Qualitative Interview

Visit	Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Week 4	28	2	56

Table 3-5. Analysis Visit Windows for Additional Study Specific Questions

Visit	Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Baseline		(none)	1
Week 4	28	2	56

3.7.3. PK Analysis Visits

For PK analysis, the nominal visit as recorded on the CRF will be used when data are summarized by visit.

Any data relating to unscheduled visits will not be assigned to a particular visit or time point and in general will not be included in by-visit summaries. However, the following exceptions will be made:

- An unscheduled visit prior to the first dosing of study drug may be included in the calculation of the baseline value, if applicable.

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

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

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

- For baseline, the last nonmissing value on or prior to the B/F/TAF will be selected, unless specified differently. If there are multiple records with the same time or no time recorded on the same day, the baseline value will be the average of the measurements for continuous data, or the measurement with the lowest severity for categorical data.

- For postbaseline values:

  — The record closest to the nominal day for that visit will be selected with the exception of viral load, CD4 cell counts, and CD4%, in which the latest record will be selected.

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

- If there is more than 1 record on the selected day, the average will be taken for continuous data (except for HIV-1 RNA, see below) and the worse severity will be taken for categorical data.

- For postbaseline HIV-1 RNA, the latest (considering both date and time) record(s) in the window will be selected.

  - If both "HIV-1 RNA COBAS 6800" and "HIV RNA REPEAT COBAS" (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 COBAS" will be selected for analysis purposes; otherwise, if there are multiple "HIV-1 RNA COBAS 6800" records with the same collection time, the geometric mean will be taken for analysis purposes.

Since the administration of PROs is limited to specific time points, there should not be any instances of conflicting multiple baseline records. If, despite expectations, conflicting multiple baseline records occur, such instances should be queried. Instances where there are multiple records within an analysis window are handled according to the PRO guidance specified in Section 9.2.

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

- For baseline, the last available record on or prior to the first dose date of study drug will be selected. If there are multiple records with the same time or no time recorded on the same day, the value with the lowest severity will be selected.

- For postbaseline visits, the most conservative value within the window will be selected.

4. PARTICIPANT DISPOSITION

4.1. Participant Enrollment and Disposition

A summary of participant enrollment will be provided for each country, investigator within a country, and overall. The summary will present the number and percentage of participants enrolled. For each column, the denominator for the percentage calculation will be the total number of participants analyzed for that column.

A summary of participant disposition will be provided by overall. This summary will present the number of participants screened, the number of participants who met all eligibility criteria but were not enrolled with reasons for participants not enrolled, the number of participants enrolled, and the number of participants in each of the categories listed below:

- Full Analysis Set
- Safety Analysis Set
- Completed study drug
- Did not complete study drug with reasons for premature discontinuation of study drug
- Completed study
- Did not complete the study with reasons for premature discontinuation of study.

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

The following by-participant listings will be provided by participant identification (ID) number in ascending order to support the above summary tables:

- Participant disposition, including, date of enrollment, first dose date and day, last dose date and day, end of study date and day, study drug discontinuation, study discontinuation, and reasons for study drug or study discontinuation.
- Reasons for screen failure (will be provided by screening ID number in ascending order).

4.2. Extent of Study Drug Exposure and Adherence

Extent of exposure to study drug will be examined by assessing the total duration of exposure to study drug and the level of adherence relative to the study drug regimen specified in the protocol.

4.2.1. Duration of Exposure to Study Drug

Total duration of exposure to study drug will be defined as last dosing date minus first dosing date plus 1, regardless of any temporary interruptions in study drug administration, and will be expressed in weeks using up to 1 decimal place (eg, 4.5 weeks). If the last study drug dosing date is missing, the latest date among the study drug end date, clinical visit dates, laboratory sample collection dates, and the vital signs assessment dates that occurred during the on-treatment period will be used for that participant included in the final analyses.

The duration of exposure to study drug will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) and as the number and percentage of participants exposed for specified periods, eg, ≥ 4 weeks (28 days), ≥ 8 weeks (56 days), ≥ 12 weeks (84 days), ≥ 24 weeks (168 days), etc.

Summaries will be provided by overall participants for the Safety Analysis Set.

No formal statistical testing is planned.

4.2.2. Adherence to Study Drug

Study drug regimen adherence will be computed based on pill counts. The numbers of pills of study drug B/F/TAF dispensed and returned are captured on study drug accountability eCRF.

Adherence (%) of B/F/TAF will be calculated as follows:

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

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

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

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

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

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

Overall adherence to study drug will be calculated using all data from the entire dosing period up to the date of permanent discontinuation of the study drug for participants who prematurely discontinued study drug or completed study drug.

Adherence up to Week 12 will be calculated using all data from the entire dosing period up to the date of permanent discontinuation of the study drug for participants who prematurely discontinued study drug or completed study drug, or the Week 12 study drug dispensing date, whichever occurs earliest.

Descriptive statistics for overall adherence and adherence up to Week 12 for the study drug (n, mean, SD, median, Q1, Q3, minimum, and maximum) along with the number and percentage of participants belonging to adherence categories (e.g., $< 80\%$, ≥ 80 to $< 90\%$, $\geq 90\%$ to $< 95\%$, $\geq 95\%$) will be provided for the Safety Analysis Set. No formal statistical testing is planned.

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

4.3. Protocol Deviations

If there are any participants did not meet the eligibility criteria for study entry but enrolled in the study, then will be summarized regardless of whether they were exempted by the sponsor or not. The summary will present the number and percentage of participants who did not meet at least 1 eligibility criterion and the number of participants who did not meet specific criteria by treatment group based on the All Enrolled Analysis Set. A by-participant listing will be provided for those participants who did not meet at least 1 eligibility (inclusion or exclusion) criterion. The listing will present the eligibility criterion (or criteria if more than 1 deviation) that participants did not meet and related comments, if collected.

Protocol deviations occurring after participants entered the study are documented during routine monitoring. The number and percentage of participants with at least 1 important protocol deviation will be summarized by deviation category for the All Enrolled Analysis Set as appropriate. The total number of important protocol deviations will be summarized by deviation category A by-participant listing will be provided for those participants with protocol deviations, included a column specify whether the protocol deviation is important.

5. BASELINE CHARACTERISTICS

5.1. Demographics and Baseline Characteristics

Participant demographic variables (ie, age, sex, gender identity, sexual orientation, race, and ethnicity) and baseline characteristics (body weight [in kg], height [in cm], body mass index [BMI; in kg/m^2]) will be summarized by overall using descriptive statistics for continuous variables and using number and percentage of participants for categorical variables. The summary of demographic data will be provided for the Safety Analysis Set. Missing values will not be included in the denominator when calculating percentages.

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

5.2. Other Baseline Characteristics

The following baseline disease characteristics will be summarized by overall using descriptive statistics for continuous variables and using number and percentage of participants for categorical variables.

- HIV-1 RNA categories (copies/mL): (a) < 50, (b) ≥ 50
- CD4 cell counts (/uL)
- CD4 cell counts categories (/uL): (a) < 50, (b) ≥50 to < 200, (c) ≥ 200 to < 350, (d) ≥ 350 to < 500, and (e) ≥ 500
- CD4 percentage (%)
- Mode of infection (HIV infection risk factors)
- HIV disease status: AIDS, asymptomatic, or symptomatic HIV infection
- $eGFR_{CG}$ (mL/min)
- HBV Surface Antigen Status
- HBV Core Antibody Status
- HCV Antibody Status
- Duration of baseline CAB+RPV exposure (year)
- Time between last dose date of baseline CAB+RPV and first dose date of study drug (days)
- Historical HIV-1 genotype resistance results: INSTI (Yes/No/Data Not Available), NNRTI (Yes/No/Data Not Available), NRTI (Yes/No/Data Not Available), PI (Yes/No/Data Not Available).

These baseline characteristics will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) for continuous data and using number and percentage of participants for categorical variables. The summary of these baseline characteristics will be provided for the Safety Analysis Set. No formal statistical testing is planned.

A by-participant listing of other baseline characteristics will be provided by participant ID number in ascending order.

5.3. Medical History

Medical history will be collected at screening. Medical history will be coded using the current Medical Dictionary for Regulatory Activities (MedDRA) dictionary.

A by-participant listing of medical history will be provided for all participants by participant ID number in ascending order.

6. EFFICACY ANALYSES

Efficacy data will be summarized for the participants in the FAS. For the FAS, all efficacy data, including data collected after the last dose of study drug, will be included, unless specified otherwise.

6.1. Efficacy Endpoints

The secondary efficacy endpoints of this study are:

- The proportion of participants with HIV-1 RNA ≥ 50 copies/mL at Weeks 12 and 24 as determined by Missing = Excluded (M = E) and Discontinuation = Failure (D = F) approach
- The proportion of participants with HIV-1 RNA < 50 copies/mL at Weeks 12 and 24 as determined by Missing = Excluded (M = E) and Discontinuation = Failure (D = F) approach
- The number and proportion of participants who prematurely discontinued B/F/TAF by Weeks 12 and 24

Additional efficacy endpoints of this study are:

- The change from baseline in CD4+ cell counts and CD4% at Weeks 12 and 24.

6.2. Analysis of the Secondary Efficacy Endpoints

6.2.1. HIV-1 RNA ≥ 50 or < 50 copies/mL at Weeks 12 and 24 as determined by Missing=Excluded and Discontinuation=Failure approach

Number and percentage of participants with HIV-1 RNA ≥ 50 copies/mL and < 50 copies/mL by visit will be analyzed using the following 2 methods for imputing missing HIV-1 RNA:

- Missing = Excluded (M = E):

  In this approach, missing data will be excluded in the computation of the percentages (ie, missing data points will be excluded from both the numerator and denominator in the computation). The denominator for percentages at a visit is the number of participants in the FAS with nonmissing HIV-1 RNA value at that visit.

- Discontinuation = Failure (D = F):

  In this approach, treatment discontinuation-as-failure analysis includes participants with at least one HIV-1 RNA value within an analysis window (see Table 3-1.) and participants who discontinued B/F/TAF before the lower bound of the analysis window. All participants who discontinued B/F/TAF before the lower bound of the analysis window will be classified in the category ‘HIV-1 RNA ≥ 50 copies/mL’ (ie, virologic failure). Missing data in the analysis window due to the other reasons will be excluded from both denominator and numerator for D = F analysis.

For both M = E and D = F analyses, the number and percentage of participants with HIV-1 RNA in the following categories will be summarized based on the FAS:

- < 50 copies/mL
  - < 20 copies/mL
    - < 20 copies/mL Not Detectable
    - < 20 copies/mL Detectable
  - 20 to < 50 copies/mL
- ≥ 50 copies/mL
  - 50 to < 200 copies/mL
  - 200 to < 400 copies/mL
  - 400 to < 1000 copies/mL
  - ≥ 1000 copies/mL
  - Discontinuation (only applicable to D = F analysis)

The proportion of participants with HIV-1 RNA < 50 or ≥ 50 copies/mL as defined by the 2 different missing data imputation methods will be summarized using descriptive statistics. Their 2-sided 95% CIs of the proportion will be constructed using the Clopper-Pearson Exact method.

For the D = F analysis, results will be summarized for Weeks 12, 24 and all other visits up to Week 24, For the M = E analysis results will be summarized for Weeks 12, 24 and all other visits with available data through the study.

For the D = F analysis, the proportion of participants with HIV-1 RNA < 50 copies/mL will be plotted for all visits up to Week 24 using the FAS. For the M = E analysis, the proportion of participants with HIV-1 RNA < 50 copies/mL will be plotted for all visits through the study .

6.2.2. Treatment Persistence

Persistence with B/F/TAF

- Persistence with B/F/TAF at Week 12 is defined as having received B/F/TAF for ≥ 57 days (i.e. the lower bound of the Week 12 visit window) and will be calculated as the proportion of participants remaining on B/F/TAF within the Week 12 analysis visit window in the FAS. Participants who prematurely discontinued from the study drug and then started the post ARV and have received B/F/TAF (including study and commercial drugs) for ≥ 57 days are considered as persistence with B/F/TAF at Week 12.

- Persistence with B/F/TAF at Week 24 is defined as having received B/F/TAF for ≥ 127 days (i.e. the lower bound of the Week 24 visit window) and will be calculated as the proportion of participants remaining on B/F/TAF within the Week 24 analysis visit window in the FAS. Participants who prematurely discontinued from the study drug and then started the post ARV and have received B/F/TAF (including study and commercial drugs) for ≥ 127 days are considered as persistence with B/F/TAF at Week 24.

Non-persistence with B/F/TAF

- Non-persistence with B/F/TAF at Week 12 will be calculated as the proportion of participants who prematurely discontinue B/F/TAF by Weeks 12 Visit (ie, prematurely discontinued B/F/TAF and having received B/F/TAF for < 57 days) in the FAS.

- Non-persistence with B/F/TAF at Week 24 will be calculated as the proportion of participants who prematurely discontinue B/F/TAF by Weeks 24 Visit (ie, prematurely discontinued B/F/TAF and having received B/F/TAF for < 127 days) in the FAS.

Treatment persistence and non-persistence will be summarized. Their 2-sided 95% CIs of the proportion will be constructed based on the Clopper-Pearson exact method.

Reason for B/F/TAF premature discontinuation during the study will be listed.

6.3. Analysis of the Additional Efficacy Endpoints

6.3.1. Analysis of CD4 Cell Counts and CD4 Percentages

The change from baseline in CD4 cell counts and CD4 percentages will be summarized by visit for participants in the FAS based on observed, on-treatment data (ie, data collected up to 1 day after the last dose date of B/F/TAF) using descriptive statistics.

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

6.4. Change From Protocol-Specified Efficacy Analyses

There are no deviations from the protocol-specified efficacy analyses.

7. SAFETY ANALYSES

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

7.1. Safety Endpoints

The co-primary endpoints of this study are:

- Proportion of participants experiencing treatment-emergent Grade 3 or 4 study drug-related adverse events (AEs) through Week 12
- Proportion of participants experiencing treatment-emergent Grade 3 or 4 laboratory abnormalities through Week 12.

The secondary safety endpoints of this study are:

- Proportion of participants experiencing treatment-emergent Grade 3 or 4 study drug-related adverse events (AEs) through Week 24
- Proportion of participants experiencing treatment-emergent grade 3 or 4 laboratory abnormalities through Week 24.

7.2. Adverse Events and Deaths

7.2.1. Adverse Events Dictionary

Clinical and laboratory adverse events (AEs) will be coded using the current version of MedDRA. System organ class (SOC), high-level group term (HLGT), high-level term (HLT), preferred term (PT), and lowest-level term (LLT) will be provided in the AE dataset.

7.2.2. Adverse Event Severity

Adverse events are graded by the investigator or qualified sub-investigator as Grade 1, 2, 3, 4, or 5 according to Division of AIDS (DAIDS) Toxicity Grading Scale, Version 2.1. For each episode, the highest grade attained should be reported as defined in the Toxicity Grading Scale. The severity grade of events for which the investigator did not record severity will be categorized as “missing” for tabular summaries and data listings. The missing category will be listed last in summary presentation.

7.2.3. Relationship of Adverse Event to Study Drug

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

7.2.4. Relationship of Adverse Events to Study Procedures

Study procedure related AEs are those for which the investigator selected "Yes" on the AE case report form (CRF) to the question of "Related to Study Procedures." Relatedness will always default to the investigator's choice, not that of the medical monitor. Events for which the investigator did not record relationships to study procedure will be considered related to study procedure for summary purposes. However, by-participant data listings will show the relationship as missing.

7.2.5. Serious Adverse Events

An SAE is defined as an event that, at any dose, results in the following:

- Death
- A life-threatening situation (Note: the term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it were more severe.)
- In-patient hospitalization or prolongation of existing hospitalization.
- Persistent or significant disability/incapacity.
- A congenital anomaly/birth defect.
- A medically important event or reaction: such events may not be immediately life – threatening or result in death or hospitalization but may jeopardize the participant or may require intervention to prevent 1 of the other outcomes constituting SAEs. Medical and scientific judgment must be exercised to determine whether such an event is reportable under expedited reporting rules. Examples of medically important events include intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization; and development of drug dependency or drug abuse.

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

7.2.6. Treatment-Emergent Adverse Events

7.2.6.1. Definition of Treatment-Emergent Adverse Events

Treatment-emergent adverse events (TEAEs) are defined as:

- Any AEs with onset date on or after the study drug start date and no later than 30 days after the study drug stop date; or
- Any adverse event leading to study drug discontinuation.

7.2.6.2. Incomplete Dates

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

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

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

7.2.7. Summaries of Adverse Events and Deaths

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

7.2.7.1. Summaries of AE incidence in Combined Severity Grade Subsets

- A brief, high-level summary of the number and percentage of participants who experienced at least 1 TEAE during the study (ie, through Week 24) in the categories described below will be provided. All deaths observed in the study will also be included in this summary.
- In addition, a brief, high-level summary of TEAEs up to the nominal Week 12 visit will be provided. Any TEAE onset date was on or before the nominal Week 12 visit date will be included.

— If TEAE onset date is partial, the onset date is on or before the month and year (or year alone) of nominal Week 12 visit, will be included as on or before nominal week 12. If the TEAE onset date is completely missing, will be included as well.

— If participants discontinued the study before Week 12 visit, all TEAEs will be included.

The number and percentage of participants who experienced at least 1 TEAE will be provided and summarized by SOC, HLT (if applicable), PT as follows:

- TEAEs during the whole study period (ie, through Week 24)
- TEAEs up to the nominal Week 12 visit (ie, through Week 12).
- For the AE categories described below, summaries will be provided by SOC and PT as follows for (i) the whole study period (ie, through Week 24), and (ii) up to the nominal Week 12 visit (ie, through Week 12).
- TEAEs with Grade 3 or higher
- TE treatment-related AEs
- TE treatment-related AEs with Grade 3 or higher
- TE SAEs
- TE treatment-related SAEs
- TEAEs leading to premature discontinuation of study drug
- TEAEs leading to premature discontinuation of study.

Multiple events will be counted only once per participant 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 worst severity will be used for those AEs that occurred more than once in an individual participant during the study.

In addition to the above summary tables, all TEAEs, TE SAEs, TE treatment-related AEs, and TE treatment-related SAEs will be summarized by PT only, in descending order of total frequency.

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

- All AEs, indicating whether the event is treatment emergent,
- All AEs up to nominal Week 12 visit, indicating whether the event is treatment emergent

- All AEs with severity of Grade 3 or higher
- All SAEs
- All treatment-related AEs
- All Deaths
- All SAEs leading to death (i.e., outcome of death)
- All AEs leading to premature discontinuation of study drug
- All AEs leading to premature discontinuation of study.

7.2.8. Additional Analysis of Adverse Events

7.3. Laboratory Evaluations

Laboratory data collected during the study will be analyzed and summarized using both quantitative and qualitative methods. The analysis will be based on values reported in conventional units. When values are below the LOQ, they will be listed as such, and the closest imputed value will be used for the purpose of calculating summary statistics as specified in Section 3.7.

Summaries of laboratory data will be provided for the Safety Analysis Set and will include data collected up to the date of the last dose of study drug plus 30 days.

A by-participant listing for laboratory test results will be provided by participant ID number and visit in chronological order for hematology, serum chemistry, and urinalysis separately for all data collected during 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. The listing will include derived visit information of the study (ie, derived visit and study day).

No formal statistical testing is planned on laboratory data.

7.3.1. 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 and percentage change from baseline each postbaseline analysis window (if specified).

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

Median (Q1, Q3) of the observed and change from baseline values for specified laboratory tests will be plotted using a line plot by treatment group and visit.

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.7.4.

7.3.2. Graded Laboratory Values

The DAIDS Toxicity Grading Scale, Version 2.1 will be used to assign toxicity grades (0 to 4) to laboratory results for analysis. Grade 0 includes all values that do not meet the criteria for an abnormality of at least Grade 1. For laboratory tests with criteria for both increased and decreased levels, analyses for each direction (ie, increased, decreased) will be presented separately.

7.3.2.1. Treatment-Emergent Laboratory Abnormalities

Treatment-emergent laboratory abnormalities are defined as values that increase at least 1 toxicity grade from baseline at any time after baseline and up to and including the date of last dose of study drug plus 30 days, will be summarized. The incidence of treatment-emergent laboratory abnormalities and Grade 3 and 4 laboratory abnormalities will also be summarized. If baseline data are missing, any graded abnormality (ie, at least a Grade 1) will be considered treatment emergent). The maximum postbaseline toxicity grade will be summarized by laboratory parameter.

7.3.2.2. Summaries of Laboratory Abnormalities

Laboratory data that are categorical will be summarized using the number and percentage of participants in the study with the given response at baseline and each scheduled postbaseline visit. Participants will be categorized according to the most severe postbaseline abnormality grade for a given lab test.

The following summaries (number and percentage of participants) for treatment-emergent laboratory abnormalities will be provided by lab test and treatment group:

- Graded treatment-emergent laboratory abnormalities during the study (ie, through Week 24)
- Graded treatment-emergent laboratory abnormalities through Week 12
- Grade 3 and 4 treatment-emergent laboratory abnormalities during the study (ie, through Week 24)

- Grade 3 and 4 treatment-emergent laboratory abnormalities through Week 12.

For all summaries of laboratory abnormalities, the denominator is the number of participants with nonmissing postbaseline values during the time period specified in Section 7.2.

Laboratory abnormalities that occur before the first dose of study drug or after the participant has been discontinued from treatment for at least 30 days will be included in a data listing. Treatment-emergent laboratory abnormalities will be flagged.

A by-participant listing of treatment-emergent Grade 3 or 4 laboratory abnormalities will be provided by participant ID number and visit in chronological order. This listing will include all test results that were collected throughout the study for the lab test of interest, with all applicable severity grades abnormal flags displayed.

7.3.3. Metabolic Laboratory Evaluations

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

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

7.3.4. Liver-related Laboratory Evaluations

Liver-related abnormalities after initial study drug dosing will be examined and summarized using the number and percentage of participants who were reported to have the following laboratory test values for (1) postbaseline measurements through Week 12 and (2) postbaseline measurements during the study (ie, through Week 24):

- Aspartate aminotransferase (AST): (a) > 3 times of the upper limit of reference range (ULN); (b) > 5 x ULN; (c) > 10 x ULN; (d) > 20 x ULN
- Alanine aminotransferase (ALT): (a) > 3 x ULN; (b) > 5 x ULN; (c) > 10 x ULN; (d) > 20 x ULN
- AST or ALT: (a) > 3 x ULN; (b) > 5 x ULN; (c) > 10 x ULN; (d) > 20 x ULN
- Total bilirubin: (a) > 1 x ULN; (b) > 2 x ULN
- Alkaline phosphatase (ALP) > 1.5 x ULN
- AST or ALT > 3 x ULN and total bilirubin: (a) > 1.5 x ULN; (b) > 2 x ULN
- AST or ALT > 3 x ULN and total bilirubin: > 2 x ULN and ALP < 2 x ULN

The summary will include data from all postbaseline visits during the time period specified in Section 7.2. For individual laboratory tests, participants will be counted once based on the most severe postbaseline values. For both the composite endpoint of AST or ALT and total bilirubin, participants will be counted once when the criteria are met at the same postbaseline visit date. The denominator is the number of participants in the Safety Analysis Set who have nonmissing postbaseline values of all relevant tests at the same postbaseline visit date. A listing of participants who met at least 1 of the above criteria will be provided.

7.3.5. Renal-related Laboratory Evaluations

7.3.5.1. Serum Creatinine and $eGFR_{CG}$

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

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

7.4. Body Weight, Height, and Vital Signs

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

- Baseline value
- Values at each postbaseline analysis window
- Change from baseline at each postbaseline analysis window.

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

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.7.4. No formal statistical testing is planned.

A by-participant listing of vital signs will be provided by participant ID number and visit in chronological order. Body weight, height, and BMI will be included in the vital signs listing, if space permits. If not, they will be provided separately.

7.5. Prior and Concomitant Medications

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

7.5.1. Nonstudy Drug Antiretroviral Medications

Any nonstudy drug ARV medications used prior to, during, or after the study (if collected) will be coded using the Gilead-modified World Health Organization (WHO) Drug Dictionary for

ARV medications. All nonstudy drug ARV medications will be listed. Post study ARVs after participants who prematurely discontinued or completed the study drug (B/F/TAF) will be summarized.

7.5.2. Concomitant Non-ARV Medications

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

For the purposes of analysis, any medications with a start date prior to or on the first dosing date of study drug and continued to be taken after the first dosing date or started after the first dosing date but prior to or on the last dosing date of study drug will be considered concomitant medications. Medications started and stopped on the same day as the first dosing date or the last dosing date of study drug will also be considered concomitant. Medications with a stop date prior to the date of first dosing date of study drug or a start date after the last dosing date of study drug will be excluded from the concomitant medication summary. If a partial stop date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) prior to the date of first study drug administration will be excluded from the concomitant medication summary. If a partial start date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) after the study drug stop date will be excluded from the concomitant medication summary. Medications with completely missing start and stop dates will be included in the concomitant medication summary, unless otherwise specified. Summaries will be based on the Safety Analysis Set. No formal statistical testing is planned.

Summaries of non-ARV concomitant medications will be provided for the Safety Analysis Set. Participants with any concomitant non-ARV medications will be listed. No inferential statistics will be provided.

7.6. Other Safety Measures

A by-participant listing of participant pregnancies during the study will be provided by participant ID number.

Although not necessarily related to safety, a by-participant listing of all comments received during the study on the comments form will be provided by participant ID number, and form for which the comment applies.

7.7. Changes From Protocol-Specified Safety Analyses

There are no deviations from the protocol-specified safety analyses.

8. PHARMACOKINETIC (PK) ANALYSES

PK samples will be collected for only participants from Northen American sites. French participants will not be included as part of the planned PK analysis.

8.1. PK Analysis Endpoint

The PK analysis endpoint which is included as part of secondary endpoint of this study is:

- Plasma concentration of BIC, CAB, and RPV at Day 1, Weeks 4, 12 and 24, as appropriate.

8.2. Trough and Single Postdose PK Sample Collection

A single PK plasma sample will be collected at Day 1 prior to dose. A single trough plasma PK sample approximately 23 to 24 hours after the previous B/F/TAF dose and prior to B/F/TAF dosing on Weeks 4, 12, and 24, and a single plasma PK sample at approximately 2 hours post B/F/TAF dose, witnessed by study staff, at Weeks 4, 12, and 24 will be collected.

8.3. PK Analyses on Trough and Postdose PK Concentrations

Natural logarithmic transformations will be used for analyzing plasma concentrations of BIC, CAB and RPV. Concentration values (including trough and postdose PK concentration) that are below the lower limit of quantitation (BLQ) will be presented as "BLQ" in the concentration listing and will be treated as zero at each time point for summary purposes.

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

- If at least 1 participant has a concentration value of BLQ for the time point, the minimum value will be displayed as "BLQ."
- If more than 25% of the participants have a concentration value of BLQ for a given time point, the minimum and Q1 values will be displayed as "BLQ."
- If more than 50% of the participants have a concentration value of BLQ for a given time point, the minimum, Q1, and median values will be displayed as "BLQ."
- If more than 75% of the participants have a concentration value of BLQ for a given time point, the minimum, Q1, median, and Q3 values will be displayed as "BLQ."
- If all participants have concentration values of BLQ for a given time point, all order statistics (minimum, Q1, median, Q3, and maximum) and summary statistics will be displayed as "BLQ."

Individual participant PK concentration data, including CAB and RPV for Day 1 (pre-dose), as well as BIC, CAB, and RPV for sparse trough and postdose PK concentrations will be listed and summarized at each time point for each analyte (as applicable) using descriptive statistics for subjects in the PK analysis set. The descriptive statistics (sample size, mean, SD, coefficient of variation [% CV], minimum, median, maximum, Q1, and Q3), will be presented for plasma concentration data. For concentration values BLQ, the number of subjects with values of BLQ will be presented.

The following tables will be provided for each analyte (ie, BIC, CAB, and RPV) using the associated PK Analysis Set:

- Individual participant concentration data and summary statistics at all protocol-specified PK sampling time points for each analyte (as applicable).

The following figures may be provided for each analyte (ie, BIC, CAB, and RPV) using the associated PK Analysis Set as appropriate:

- Mean (± SD) concentration data versus time (on linear and semilogarithmic scales). If more than one-third of the values at a postdose timepoint are BLQ or less than 5 participants presented at the timepoint then the mean and SD will not be presented at that time point and remaining points connected. If lower error bar (mean-SD) is < 0 at a timepoint then it will not be presented at that timepoint.
- Median (Q1, Q3) concentration data versus time (on linear and semilogarithmic scales). If more than one-third of the values at a postdose timepoint are BLQ or less than 5 participants presented at the timepoint then the median and quartile values will not be presented at that timepoint, and remaining points connected. If lower error bar (Q1) is BLQ at a timepoint then it will be presented as lower LOQ at that timepoint.

The following listings will be provided:

- PK sampling details by participant, including procedures, differences in scheduled and actual draw times, and sample age from the PK samples. Day1 (pre-dose), trough PK samples and postdose PK samples will be marked separately in the listing.

8.4. Sensitivity Analysis

A sensitivity analysis will be conducted by only including the participants who have received the study drugs per the protocol. In this scenario, the PK data will be presented as the overall summary and based on data from the participants that have received the study drugs per the protocol as part of the sensitivity analysis. Specifically, for participants who were on CAB+RPV IM injections twice monthly (Q2M) prior to enrollment but received first dose of the study drug (B/F/TAF) < 46 days of the last dose of CAB+RPV IM injection, their PK data will be excluded from the summary statistics in the sensitivity analysis.

8.5. Changes From Protocol-Specified PK Analyses

There are no deviations from the protocol-specified PK analyses.

9. ANALYSIS ON PARTICIPANT-REPORTED OUTCOMES

Participant Reported Outcomes (PRO) will be analyzed based on the Full Analysis Set using all PRO data collected on-treatment (ie, data collected up to 1 day after the last dose date of B/F/TAF), which involve the following data:

- The HIV Treatment Satisfaction Questionnaire Status (HIVTSQs) are to be completed by participants at Day 1 (Baseline) and Weeks 12 and 24. The HIV Treatment Satisfaction Questionnaire Change (HIVTSQc) are to be completed by participants at Week 4.

- A study-specific questionnaire will be completed by participants on Day 1 and week 4 to document preference for oral vs injection therapy and specific reasons for decisions to switch from CAB+ RPV to oral therapy.

Any PRO data collected not on-treatment will be listed and flagged in the listings.

9.1. Patient-Reported Outcomes

The PRO related secondary endpoint include:

- Change in HIV treatment satisfaction (HIVTSQc) score at Week 4.

The PRO related other endpoint include:

- Total score and change from baseline in HIVTSQs at Week 12 and 24.

The PRO related exploratory endpoints include:

- Week 12 reported experiences with CAB+RPV, reasons for switch to B/F/TAF, preferences for injectable and oral therapy from qualitative interviews of participant experience

- Participant-reported perceptions of CAB+RPV treatment, reasons for switch to B/F/TAF.

9.2. Analysis Methods

9.2.1. HIV Treatment Satisfaction Status (HIVTSQs) and HIV Treatment Satisfaction Change (HIVTSQc)

The HIVTSQ "status version" (**HIVTSQs**, see Appendix 3) measures participants satisfaction with their current treatment. Participants respond to the HIVTSQ items using a Likert scale ranging from 0 to 6, where 0 represents the least favourable option ("very dissatisfied") and 6 represents the most favourable option ("very satisfied"). See Appendix 3 for study specific questionnaire. A treatment satisfaction scale total will be calculated as the sum of the responses to the first 11 items on the **HIVTSQs** form (range from 0 to 66), where higher scores indicate a greater level of satisfaction with their HIV-1 treatment. Item 12 (pain/discomfort) will be treated as an individual item score.

The HIVTSQ "change version" (**HIVTSQc**, see Appendix 3) was designed to assess the change in treatment satisfaction between a participant's previous and current treatment. The individual items are scored from −3 ("much less satisfied now") to 3 ("much more satisfied now"). A treatment satisfaction scale total in change will be calculated as the sum of the responses to the first 11 items on the **HIVTSQc** form (range from -33 to 33), where higher scores indicate a greater improvement in treatment satisfaction with the new treatment, and lower scores indicate lower treatment satisfaction with the new treatment, and a score of zero represents no change in satisfaction. Item 12 (pain/discomfort) will be treated as an individual item score (Reference 1).

If a question is scaled more than once, then the average will be used for in-between choices (eg, use 2.5 if 2 and 3 are answered for the same question). If the two answers are not consecutive, then the answer will be treated as missing value (eg, use "missing" if 2 and 5 are answered for the same question). Missing values will not be imputed.

The following tables will be provided using the Full Analysis Set:

- Individual measurement of HIVTSQs by visit while receiving study drug (B/F/TAF)
- Summary of HIVTSQs total score and change from baseline by visit while receiving study drug (B/F/TAF)
- Individual measurement of HIVTSQc at Week 4 while receiving study drug (B/F/TAF)
- Summary of HIVTSQc total score at Week 4 while receiving study drug (B/F/TAF).

The HIVTSQs scale totals at Day 1 (Baseline), Weeks 12 and 24, and the HIVTSQc scale totals at Week 4 will be summarized using descriptive statistics (sample size, mean, SD, median, Q1, Q3, minimum, and maximum). The number and percent of participants with responses to each question will be provided at each visit.

The following figures may be provided using the Full Analysis Set:

- Mean (± SD) HIVTSQs by visit while receiving study drug (B/F/TAF)
- Mean (95% CIs) HIVTSQs by visit while receiving study drug (B/F/TAF).

In addition, by-participant listings for the numerical responses in HIVTSQs and HIVTSQc will be provided by participant ID number and visits in chronological order using the All Enrolled Analysis Set.

9.2.2. Additional Study-Specific Questions

Proportion of participants with specific reasons for each question related to participant experience with CAB + RPV will be summarized at Baseline (Day 1, see Appendix 4) and Week 4 (see Appendix 5) using the Full Analysis Set in the following summary tables:

- Study-specific Questionnaire on Day 1: Questions Related to Participant Experience with CAB + RPV
- Study-specific Questionnaire on Week 4: Questions Related to Participant Experience after switching to oral B/F/TAF.

By-participant listings of qualitative interview responses will be provided by participant ID number (in ascending order) on Day 1 and Week 4 for the Study GS-US-380-6738 Additional Questions for Participant Questionnaire and Responses using the All Enrolled Analysis Set.

10. REFERENCES

- Clare Bradley, The HIV Treatment Satisfaction Questionnaire (HIVTSQ-12) User Guidelines.
- Clare Bradley, The HIV Dependent Quality of life Questionnaire (HIVDQoL) User guidelines.
- U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER). Guidance for Industry. Bioavailability and Bioequivalence Studies for Orally Administered Drug Products - General Considerations (Revision 1). March 2003.
- U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER). Guidance for Industry. Statistical Approaches to Establishing Bioequivalence. January 2001.

11. SOFTWARE

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

12. SAP REVISION

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

13. APPENDICES

Appendix 1. Schedule of Assessments

Study Procedures	Screening[a]	Day 1[b]	Week 4[c]	Week 12[c]	Week 24[c]	30-Day Follow-up[d]	ESDD[e]	Notes
Informed Consent	X							
Medical History	X							
Concomitant Medications	X	X	X	X	X	X	X	At screening, concomitant medications taken within 30 days prior to screening will be recorded; at subsequent visits all medications since the last study visit will be recorded
Adverse Events	X	X	X	X	X	X	X	
Complete Physical Examination	X							Complete physical examination (urogenital/anorectal examinations will be performed at the discretion of the investigator)
Symptom-Directed Physical Examination		X	X	X	X	X		Symptom-directed physical examination at all post-screening time points.
Vital Signs and Weight	X	X	X	X	X	X	X	
Height	X							
Urinalysis	X	X	X	X	X	X	X	
Urine Pregnancy		X	X	X	X	X	X	For participants of childbearing potential only
Serum Pregnancy	X							For participants of childbearing potential only
Chemistry Profile[f]	X	X	X	X	X	X	X	
Hematology Profile	X	X	X	X	X	X	X	CBC with differential and platelet count
CD4+ Cell Count	X	X		X	X		X	
Plasma HIV-1 RNA[g]	X	X	X	X	X	X	X	
HBV and HCV Serologies[h]	X							
Estimated GFR	X	X		X	X		X	Estimated GFR according to the Cockcroft-Gault formula for creatinine clearance
Metabolic Assessments[i]		X		X	X			
Baseline PK, Sparse PK: trough and postdose PK sample[j]		X	X	X	X			

Study Procedures	Screening[a]	Day 1[b]	Week 4[c]	Week 12[c]	Week 24[c]	30-Day Follow-up[d]	ESDD[e]	Notes
Plasma Storage Sample[k]		X	X	X	X		X	
Whole Blood sample for potential HIV DNA genotyping		X						Whole blood sample for virology analysis
Plasma HIV-1 genotyping/phenotyping sample[l]			X	X	X		X	HIV-1 genotype/phenotype resistance testing for participants with unconfirmed virologic rebound with HIV-1 RNA value ≥ 200 copies/mL
Dried Blood Spot (DBS) collection			X	X	X		X	TFV-DP from DBS will be run in retrospect for participants with confirmed viral failure
HIVTSQs		X		X	X			
HIVTSc Questionnaire			X					
Additional Quantitative Interview Questions		X	X					
Qualitative interview			X					Qualitative interview will explore in-depth experiences on CAB+RPV, reasons for switch B/F/TAF and satisfaction post switch. The visit window for the interview is from week 3 to week 9
Study Drug Accountability		X	X	X	X	X	X	
Study Drug Dispensation		X		X				
Observed Dosing		X	X	X				Participants must take their study drug in the clinic for observed dosing on Day 1, Week 4, Week 12, .

CBC = complete blood count; CD4+ = clusters of differentiation 4; DNA = deoxyribonucleic acid; DBS = dried blood spot; ESDD = early study drug discontinuation; GFR = glomerular filtration rate calculated using the Cockcroft-Gault equation; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV-1 = human immunodeficiency virus type 1; HIVTSQs = HIV treatment satisfaction status questionnaire [quantitative]; HIVTSQc = HIV treatment satisfaction change questionnaire [quantitative]; RNA = Ribonucleic acid; PK = pharmacokinetic(s); TFV-DP = tenofovir diphosphate.

a Evaluations to be completed within 42 days prior to Day 1 visit.

b Participants will be dispensed study drug at the Day 1 visit; initiation of treatment with the study drug must take place in the clinic for observed dosing at Day 1 visit.

c All study visits are to be scheduled relative to the Day 1 visit date. Visit windows are ± 2 days of the protocol-specified date through Week 12, ± 6 days of the protocol-specified date for Week 24. For the purpose of scheduling a 30-day follow-up visit, a ± 6-day window may be used. Those participants who prematurely discontinue study drug and continue in the study through at least one subsequent visit after the early study drug discontinuation visit will not be required to complete the 30-day follow-up visit.

d Only applies to participants who miss the Week 24 visit and must be completed within 30 days of discontinuing study drug.

e Early study drug discontinuation visit to occur within 72 hours of last dose of study drug.

f Chemistry profile: alkaline phosphatase, AST, ALT, total bilirubin, direct and indirect bilirubin, total protein, albumin, bicarbonate, BUN, calcium, chloride, creatinine, glucose, potassium, and sodium.

g For any post-Day -1 visit, if the HIV-1 RNA value is ≥ 50 copies/mL, a retest should be performed at a scheduled or unscheduled visit 2-4 weeks after the date of the original test.

h Hepatitis B virus surface Antigen (HBsAg), Hepatitis B core antibody (HBcAb), and Hepatitis C virus (HCV) serologies (reflex HCV RNA is performed in participants with positive HCV Ab serology)

i Metabolic Assessments: Fasting lipid panel (total cholesterol, HDL, direct LDL, triglycerides). If the participant has not fasted prior to the visit, the visit may proceed, but the participant must return within 72 hours in a fasted state.

j A single trough plasma PK sample approximately 23 to 24 hours after the previous dose and prior to dosing on Weeks 4, 12, and 24, and a single post-dose plasma PK sample at approximately 2 hours (relative to B/F/TAF dosing observed by the study staff) at Weeks 4, 12, and 24 will be collected.

k Plasma storage sample for safety, PK, and/or virology (Day 1, Weeks 4-24, and ESDD).

l l. HIV-1 genotype/phenotype resistance testing (which includes protease, reverse transcriptase, and integrase testing) only conducted for participants with confirmed virologic failure with HIV-1 RNA value ≥ 50 copies/mL. Following virologic rebound, participants 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 an HIV-1 RNA and HIV-1 genotype and phenotype blood draw. Based on the results of this testing, participants should be managed according to the Virologic Rebound Schema. Participants with HIV-1 RNA ≥ 50 copies/mL at Week 12 and/or 24 will be asked to return for an unscheduled visit within the visit window for a retest. Participants with HIV-1 RNA ≥ 200 copies/mL at ESDD, last visit, or Week 12 or 24 will also have resistance testing conducted.

Appendix 2. Laboratory Analytes

Safety Laboratory Measurements			Other Laboratory Measurements
Chemistry (Serum or Plasma)	**Hematology**	**Urinalysis**	
Alkaline phosphatase ALT AST Total bilirubin Total protein Albumin Bicarbonate BUN Calcium Chloride Serum creatinine Glucose Phosphorus Potassium Sodium Fasting lipid profile: Triglycerides Cholesterol and its subfractions (HDL and LDL)	Hematocrit Hemoglobin Platelet count RBC count RBC indices WBC count differentials (absolute and percentage), including: Leucocytes Monocytes Neutrophils Eosinophils Basophils MCV	Appearance Blood Color Glucose Leukocyte esterase Microscopy (including crystals) Nitrites pH Pregnancy Protein Specific gravity Urobilinogen	CD4+ counts DBS HBV/HCV Serologies HIV-1 RNA HIV-1 genotype/phenotype PK blood Serum Pregnancy

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CD4+ = clusters of differentiation; HDL = high-density lipoprotein; LDL = low-density lipoprotein; MCV = mean corpuscular volume; PK = pharmacokinetic(s); RBC = red blood cell; RF = rheumatoid factor; RNA = ribonucleic acid; TB = tuberculosis; TSH = thyroid-stimulating hormone; WBC = white blood cell
Refer to Appendix 1 for collection time points.

Appendix 3. Item content of the HIVTSQs and HIVTSQc

Item number	Item Label	Item Wording	Response Options for Status Form (HIVTSQs)	Response Options for Change Form (HIVTSQc)
1	Current treatment	How satisfied are you with your current treatment?	Very satisfied 6 to 0 very dissatisfied	Much more satisfied now 3 to −3 much less satisfied now
2	Control	How well controlled do you feel your HIV has been recently?	Very well controlled 6 to 0 very poorly controlled	Much better controlled now 3 to −3 much worse controlled now
3	Side effects	How satisfied are you with any side effects of your present treatment?	Very satisfied 6 to 0 very dissatisfied	Much more satisfied now 3 to −3 much less satisfied now
4	Demands	How satisfied are you with the demands made by your current treatment?	Very satisfied 6 to 0 very dissatisfied	Much more satisfied now 3 to −3 much less satisfied now
5	Convenience	How convenient have you been finding your treatment to be recently?	Very convenient 6 to 0 very inconvenient	Much more convenient now 3 to −3 much less convenient now
6	Flexibility	How flexible have you been finding your treatment to be recently?	Very flexible 6 to 0 very inflexible	Much more flexible now 3 to −3 much less flexible now
7	Understanding	How satisfied are you with your understanding of your HIV?	Very satisfied 6 to 0 very dissatisfied	Much more satisfied now 3 to −3 much less satisfied now
8	Lifestyle	How satisfied are you with the extent to which the treatment fits in with your lifestyle?	Very satisfied 6 to 0 very dissatisfied	Much more satisfied now 3 to −3 much less satisfied now
9	Recommend to others	Would you recommend your present treatment to someone who is being offered this HIV treatment?	Yes I would definitely recommend the treatment 6 to 0 No I would definitely not recommend the treatment	Much more likely to recommend the treatment now 3 to −3 much less likely to recommend the treatment now
10	Continue	How satisfied would you be to continue with your present form of treatment?	Very satisfied 6 to 0 very dissatisfied	Much more satisfied now 3 to −3 much less satisfied now
11	Easy/difficult	How easy or difficult have you been finding your treatment to be recently?	Very easy 6 to 0 very dissatisfied	Easier now 3 to −3 much less satisfied now
12	Pain/discomfort	How satisfied are you with the amount of discomfort or pain involved with your present form of treatment?	Very satisfied 6 to 0 very dissatisfied	Much more satisfied now 3 to −3 much less satisfied now

Appendix 4. Study GS-US-380-6738 Additional Questions for Participant (Questionnaire) on Day 1

Day 1: Questions related to participant experience with CAB + RPV

1. **How did you first hear about injectable CAB + RPV (Cabenuva):**
    a. From a doctor, nurse, social worker, or other health provider
    b. From a friend, relative, partner, acquaintance or other patient
    c. From an advertisement (TV, radio, internet, magazine, etc.)
    d. Internet (search, social media, etc.)
    y. Another source
2. **Which of the following factors led you to decide to take injectable CAB + RPV (Cabenuva)**
    a. A friend, relative, partner, acquaintance, or other patient recommended it
    b. A doctor, nurse, social worker, or other health practitioner
    c. Research I did on my own (such as internet searches)
    d. Advertisement (TV, radio, internet, magazine, etc.)
    e. Wanting to reduce or stop side effects from daily oral medication
    f. Fear of stigma or negative feelings from taking HIV medication every day
    g. Fear that others will be more likely to know I have HIV with daily oral medication
    h. Not needing to remember to take daily oral medication
    i. Fear of missing doses of daily oral HIV medications
    j. Wanting to forget about having HIV for a while (no reminder every day)
    k. More convenient than oral treatment
    l. I think injections would work better than daily oral medication
    m. It is a new and exciting HIV treatment
    n. Want to have more in-person contact with healthcare system

y. Another reason

3. Of the reasons listed in question 2, which would you rank as the TOP reason you started injectable CAB + RPV? (Cabenuva)?

a. A friend, relative, partner, acquaintance, or other patient recommended it

b. A doctor, nurse, social worker, or other health practitioner

c. Research I did on my own (such as internet searches)

d. Advertisement (TV, radio, internet, magazine, etc.)

e. Wanting to reduce or stop side effects from daily oral medication

f. Fear of stigma or negative feelings from taking HIV medication every day

g. Fear that others will be more likely to know I have HIV with daily oral medication

h. Not needing to remember to take daily oral medication

i. Fear of missing doses of daily oral HIV medications

j. Wanting to forget about having HIV for a while (no reminder every day)

k. More convenient than oral treatment

l. I think injections would work better than daily oral medication

m. It is a new and exciting HIV treatment

n. Want to have more in-person contact with healthcare system

z. Another reason

4. During your time taking CAB + RPV (Cabenuva), how inconvenient was it to go to the clinc/doctor's office to receive CAB+RPV (Cabenuva) injections as directed

a. Not at all inconvenient

b. A little inconvenient

c. Moderately inconvenient

d. Very inconvenient

e. Extremely inconvenient

5. **Did you reschedule any appointments for getting your CAB+RPV (Cabenuva) injections in the past 6 months**

    a. I did not reschedule any appointments

    b. I rescheduled 1-2 appointments

    c. I rescheduled 3-4 appointments

    d. I rescheduled 5 or more appointments

6. **Did you miss any appointments entirely for getting your CAB+RPV (Cabenuva) injections in the past 6 months?**

    a. I did not miss any appointment (skip to Question 8)

    b. Missed 1-2 appointments

    c. Missed 3-4 appointments

    d. Missed 5 or more appointments

7. **Did missing appointments in the last 6 months lead to receiving CAB+RPV (Cabenuva) injections late or outside the window when you were supposed to receive them?**

    a. Yes

    b. No

    c. I don't know

8. **Which of the following side effects did you experience while on CAB+RPV (Cabenuva)?**

    a. Pain from the injection

    b. Soreness from the injection

    c. Lump, bump, or nodule from the injection

    d. Swelling around the injection site

    e. Redness around the injection site

    f. Itching at the injection site

    g. Muscle aches

h. Headache

i. Nausea/upset stomach

j. Diarrhea

k. Sleep problems

l. Dizziness

m. Allergic reaction (rash, fever, blisters, tiredness, trouble breathing)

n. Fatigue/tiredness

y. Another side effect

z. I did not experience any side effects while on CAB+RPV (Cabenuva) - Skip to Question 11

9. Did you experience any side effects that affected your ability to do your daily activities?

a. Yes

b. No

10. How much did the side effects experienced while on CAB+RPV (Cabenuva) bother you?

a. They don't bother me at all

b. I am a little bothered by them

c. I am moderately bothered by them

d. I am very bothered by them

e. I am extremely bothered by them

11. Why did you decide to switch from CAB+RPV (Cabenuva) to daily oral medication B/F/TAF (Biktarvy)?

a. I didn't like the side effects of CAB+RPV (Cabenuva)

b. Visits to the clinic were too frequent

c. Waiting time in the office to get injections

d. Difficulty with insurance or cost

e. Difficulty scheduling appointments for injections

f. I want to have less in-person contact with the healthcare system

g. I have anxiety about receiving injections

h. I prefer oral medication over injections

i. A doctor, nurse, social worker, or other health practitioner said I should switch

j. A friend, relative, partner, acquaintance, or other patient said I should switch

k. I already take on other daily oral medication, so taking one more wouldn't make a difference

l. Concern that the medication in the injection might not last 2 months

m. Concern about developing resistance with CAB+RPV (Cabenuva)

n. I want to be in more control of my HIV medication

o. I took B/F/TAF (Biktarvy) before and I had a good experience with it

p. I think B/F/TAF (Biktarvy) is more effective than CAB+RPV (Cabenuva)

q. I think B/F/TAF (Biktarvy) has less side effects than CAB + RPV (Cabenuva)

y. Another reason

12. Of all the reasons you checked in question 11, which would you rank as the TOP reason you decided to switch from CAB + RPV (Cabenuva) to daily oral medication B/F/TAF (Biktarvy)?

a. I didn't like the side effects

b. Visits to the clinic were too frequent

c. Waiting time in the office to get injections

d. Difficulty with insurance or cost

e. Difficulty scheduling appointments for injections

f. I want to have less in-person contact with the healthcare system

g. I have anxiety about receiving injections

h. I prefer oral medication over injections

i. A doctor, nurse, social worker, or other health practitioner said I should switch

j. A friend, relative, partner, acquaintance, or other patient said I should switch

k. I already take on other daily oral medication, so taking one more wouldn't make a difference

l. Concern that the medication in the injection might not last 2 months

m. Concern about developing resistance with CAB + RPV (Cabenuva)

n. I want to be in more control of my HIV medication

o. I took B/F/TAF (Biktarvy) before and I had a good experience with it

p. I think B/F/TAF (Biktarvy) is more effective than CAB + RPV (Cabenuva)

q. I think B/F/TAF (Biktarvy) has less side effects than CAB + RPV (Cabenuva)

y. Another reason

13. How hopeful do you feel about starting Biktarvy in terms of successfully treating your HIV?

a. Very hopeful

b. Hopeful

c. Somewhat hopeful

d. Not hopeful at all

Appendix 5. Study GS-US-380-6730 Additional Questions for Participant (Questionnaire) on Week 4

Week 4: Questions related to participant experience after switching to oral B/F/TAF

1. **Which of the following side effects have you experienced with B/F/TAF (Biktarvy) since switching from CAB + RPV (Cabenuva)?**

   a. Headache

   b. Nausea/Upset stomach

   c. Diarrhea

   d. Sleep problems

   e. Fatigue/Tiredness

   f. Dizziness

   g. Abdominal swelling or bloating

   y. Another side effect

   z. I have not experienced any side effects with B/F/TAF (Biktarvy) (skip to question 5)

2. **Are you still experiencing any of these side effects? Please select all the side effects that still bother you at least a little.**

   a. Headache

   b. Nausea/Upset stomach

   c. Diarrhea

   d. Sleep problems

   e. Fatigue/Tiredness

   f. Dizziness

   g. Abdominal swelling or bloating

   y. Another side effect

   z. I am not still experiencing any side effects with B/F/TAF (Biktarvy) (skip to question 5)

3. **If you are still experiencing side effects from B/F/TAF (Biktarvy), have any of these side effects affected your ability to do your daily activities?**

   a. Yes

   b. No

4. **If you are experiencing side effects from B/F/TAF (Biktarvy), please rate how much the side effects bother you.**

   a. They don't bother me at all

   b. I am a little bothered by them

   c. I am moderately bothered by them

   d. I am very bothered by them

   e. I am extremely bothered by them

5. **Since you started B/F/TAF (Biktarvy), have you missed any doses? In other words, were there any days you did not take B/F/TAF (Biktarvy)?**

   a. I did not miss any doses

   b. Missed 1-2 doses

   c. Missed 3-4 doses

   d. Missed 5-6 doses

   e. Missed 7-8 doses

   f. Missed 9 or more doses

Appendix 6. Programming Specifications

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

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

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

Baseline height and weight will be used for this calculation.

2) Calcium Corrected for Albumin

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

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

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

3) Estimated GFR

The following formula will be used to calculate eGFRCG:

- eGFRCG (mL/min) = [(140 – age (yrs)) × weight (kg) × (0.85 if female)] / (SCr (mg/dL) × 72),

where weight is total body mass in kilograms, and SCr is serum creatinine.

4) Duration of Baseline CAB+RPV

Duration of Baseline CAB+RPV prior to enrollment is defined as (End Date – Start Date + 1). Duration will be expressed in years so that duration in days will be divided by 365.25 days.

- End date is defined as the first dose date of B/F/TAF – 1, or the enrollment date if enrolled but not dosed.
- Start Date: Only participants who has been on CAB+RPV IM injections (Q2M) are eligible to be enrolled to the study. Participants should have received at least one dose of CAB+RPV IM injection, with no missed CAB+RPV injections. Participants may (or may not) take oral CAB+RPV (lead in) before receiving CAB+RPV IM injections (Q2M). The start date is the first dose date of baseline CAB+RPV, regardless of oral or IM injection.