STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 2a Study to Evaluate the Safety and Tolerability of a Regimen of Dual Anti-HIV Envelope Antibodies, VRC07-523LS and CAP256V2LS, in a Sequential Regimen with a TLR7 Agonist, Vesatolimod, in Early Antiretroviral-Treated HIV-1 Clade C-Infected Women
Name of Test Drug:	Vesatolimod (VES; GS-9620)
Study Number:	GS-US-382-5445
Protocol Version (Date):	Amendment 3: 07 October 2022
Analysis Type:	Final Analysis
Analysis Plan Version:	Version 1.0
Analysis Plan Date:	11 June 2025
Analysis Plan Author(s):	PPD

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LIST OF ABBREVIATIONS

ADA	antidrug antibody
AE	adverse event
ALT	alanine aminotransferase
ART	antiretroviral therapy
ARV	antiretroviral
AST	aspartate aminotransferase
ATI	analytical treatment interruption
AUC	area under the curve
BLQ	below the limit of quantitation
BMI	body mass index
CCG	eCRF Completion Guidelines
CI	confidence interval
COVID-19	novel coronavirus
CRS	cytokine release syndrome
CTCAE	Common Terminology Criteria for Adverse Events
CV	coefficient of variation
DMC	data monitoring committee
ECG	electrocardiogram
eCRF	electronic case report form
$eGFR_{CG}$	estimated glomerular filtration rate using Cockcroft-Gault formula
ESDD	early study drug discontinuation
ET	early termination
FAS	full analysis set
FcgR	Fc gamma receptors
FRESH	Females Rising through Education, Support, and Health
GALT	gut-associated lymphoid tissue
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HIV-1	human immunodeficiency virus type 1
HLGT	high-level group term
HLT	high-level term
ISG	interferon-stimulated gene
ID	identification
IV	intravenous
LLT	lower-level term
LLOQ	lower limit of quantitation
LOQ	limit of quantitation

MST	MedDRA search term
MedDRA	Medical Dictionary for Regulatory Activities
NLP	Natural Language Processing
PBMC	peripheral blood mononuclear cell
PK	pharmacokinetics
PrEP	preexposure prophylaxis
PS	Patient Safety
PT	preferred term
Q1, Q3	first quartile, third quartile
RNA	ribonucleic acid
SAP	statistical analysis plan
SAE	serious adverse events
SD	standard deviation
SE	standard error
SNP	single nucleotide polymorphism
SOC	system organ class
TE	treatment-emergent
TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
TLR	toll-like receptor
ULOQ	upper limit of quantitation
VES	Vesatolimod
WHO	World Health Organization

PHARMACOKINETIC ABBREVIATIONS

AUC_{inf}	area under the concentration versus time curve extrapolated to infinite time, calculated as $AUC_{last} + (C_{last}/\lambda z)$
AUC_{last}	area under the concentration versus time curve from time zero to the last quantifiable concentration
AUC_{exp}	area under the concentration versus time curve extrapolated between AUC_{last} and AUC_{inf}
C_{last}	last observed quantifiable concentration of the drug
C_{max}	maximum observed concentration of drug
CL	clearance following intravenous administration
CL/F	apparent oral clearance after administration of the drug: at single dose: $CL/F = Dose/AUC_{inf}$, where "Dose" is the dose of the drug
$t_{1/2}$	estimate of the terminal elimination half-life of the drug, calculated by dividing the natural log of 2 by the terminal elimination rate constant (λ_z)
T_{last}	time (observed time point) of C_{last}
T_{max}	time (observed time point) of C_{max}
V_{ss}	volume of distribution of the drug at steady state after intravenous administration
V_z	volume of distribution of the drug after intravenous administration
V_z/F	apparent volume of distribution of the drug after extravascular administration
λz	terminal elimination rate constant, estimated by linear regression of the terminal elimination phase of the concentration of drug versus time curve of the drug

1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical analysis methods and data presentations to be used in tables, figures, and listings (TFLs) in the clinical study report (CSR) for Study GS-US-382-5445. This SAP is based on the study protocol amendment 3 dated 07 October 2022 and the electronic case report form (eCRF). The SAP will be finalized before database finalization. Any changes made after the finalization of the SAP will be documented in the CSR.

1.1. Study Objectives and Endpoints

Primary Objectives	**Primary Endpoints**
• To evaluate the safety and tolerability of dual anti-HIV envelope mAbs, VRC07-523LS and CAP256V2LS, in a sequential regimen with a TLR7 agonist, VES, when administered in virologically suppressed HIV-1 Clade C-infected women on antiretroviral therapy (ART) and during analytical treatment interruption (ATI)	• The proportion of participants with treatment-emergent AEs • The proportion of participants with treatment-emergent graded laboratory abnormalities
Secondary Objectives	**Secondary Endpoints**
• To evaluate the pharmacokinetics (PK) of VRC07-523LS, CAP256V2LS, and VES • To evaluate whether VRC07-523LS and CAP256V2LS induce anti-VRC07-523LS and/or anti-CAP256V2LS antibodies • To evaluate the effect of VRC07-523LS and CAP256V2LS in a sequential regimen with VES on viral control or the need for resumption of ART following an ATI	<u>Virology/Efficacy</u> • Time to viral rebound (confirmed ≥ 50 copies/mL and ≥ 200 copies/mL) following ATI • The change in plasma viral load set-point following ATI • Viral load at the end of ATI • Time to ART resumption following ATI <u>Pharmacokinetics</u> • PK parameters for VES in plasma will include C_{max}, T_{max}, C_{last}, T_{last}, AUC_{inf}, AUC_{last}, AUC_{exp}, $t_{1/2}$, CL/F, and V_z/F. PK parameters for VRC07-523LS and CAP256V2LS in serum will include C_{max}, T_{max}, C_{last}, T_{last}, AUC_{inf}, AUC_{last}, AUC_{exp}, $t_{1/2}$, CL, V_{ss}, and V_z <u>Immunogenicity</u> • The proportion of participants with positive anti-VRC07-523LS or anti-CAP256V2LS antibodies


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1.2. Study Design

Design Configuration and Participant Population

This is a phase 2a, open-label, single-center, single-arm study to evaluate a sequential regimen of dual mAbs, VRC07-523LS and CAP256V2LS, with a toll-like receptor (TLR)7 agonist, VES, in non-pregnant, non-lactating female adults recruited from the Females Rising through Education, Support, and Health (FRESH) acute HIV infection cohort, who have HIV-1 and initiated immediate ART during acute HIV-1 infection and have been virologically suppressed (HIV-1 RNA < 50 copies/mL) on ART for at least 12 consecutive months prior to screening. Two or less unconfirmed virologic elevations of ≤ 1000 copies/mL at non-consecutive visits prior to screening are acceptable. This study will enroll up to 25 participants.

Treatment Group

This is an open-label, single-arm study. All participants will receive:

- VES 6 mg (3 x 2 mg tablets) or 8 mg (4 x 2 mg tablets), administered orally under fasted conditions.
- VRC07-523LS 20 mg/kg, intravenous (IV) infusion over 30 minutes
- CAP256V2LS 20 mg/kg, IV infusion over 30 minutes

Study Schema

Participants will attend study visits and undergo assessments over 4 periods for a maximum of 60 weeks. During Periods 1 and 2, participants will be evaluated weekly at a minimum and during Periods 3 and 4, every 2 weeks at a minimum. Vesatolimod will be dosed orally, every 2 weeks, for a total of 10 doses during Periods 1 and 2. Participants will receive the first dose of VES alone in Period 1 prior to single, sequential infusions of VRC07-523LS and CAP256V2LS administration 1 week later.

Table 1-1. Study Schema

Screening[a]	Prebaseline	Period 1[b]	Period 2[c]	Period 3[d]	End-of-Period 3 Visit[e]	Period 4[f]	ESDD and Follow-Up Procedure[g]	End-of-Study Visit[h]
		Continue ART	ATI from Day 35	ATI		4A–(ART restart[i]) or 4B (ATI Extension[j])		
≤ 35 days	Day -13	Days 0-28	Days 29-133	Days 134-336		Days 337-413		
		VES Doses 1-3[k]	VES Doses 4-10[k]	No Dosing		No Dosing		
		VRC07-523LS and CAP256V2LS Doses[l]						

ART = antiretroviral therapy; ATI = analytical treatment interruption; VES = vesatolimod

a Screening must occur 35 days prior to prebaseline/Day −13 visit.

b During Period 1, participants will have a study visit every week at a minimum over 4 weeks. Participants will continue to take their ART during this period.

c During Period 2, participants will have a study visit every week at a minimum over 15 weeks. No VRC07-523LS and CAP256V2LS dose to occur in this period. No ART will be administered and ATI will start from Day 35. If the ART restart criteria are met, the participant may stop Period 2, complete the end-of-Period 3 visit, and restart ART in Period 4A.

d During Period 3, participants will have a study visit every 2 weeks over 28 weeks. No study drug (VES, VRC07-523LS, or CAP256V2LS) will be administered in this period. No ART will be administered, and ATI will continue. If the ART restart criteria are met, the participant may stop Period 3, complete the end-of-Period 3 visit, and restart ART in Period 4A.

e The visit will be completed at the end of Period 3 or if ART restart criteria are met prior to starting Period 4A.

f Participants who have remained virologically suppressed (plasma HIV-1 RNA < 50 copies/mL) or have not met the ART restart criteria by the end of Period 3 will continue into Period 4. The option will be available for either Period 4A, restart of ART for 12 weeks, or Period 4B, to remain off ART for a 12-week ATI extension. The choice of Period 4A or 4B will be at the discretion of the participant and investigator. Participants who meet the ART restart criteria prior to the end of Period 3 may also take part in Period 4A. No study drug (VES, VRC07-523LS, and CAP256V2LS) will be administered in this period.

g If a participant should discontinue study dosing as described in Protocol Section 6.9.1, they will be required to complete an early study drug discontinuation (ESDD) visit and every attempt should be made to keep the participant in the study and continue to perform study procedures. If the participant is unable to complete all scheduled procedures, for criteria other than those described for study discontinuation in Protocol Section 3.5., the participant should be followed by telephone for a further duration of time as described in Protocol Section 6.9.2. If a participant has completed all study drug dosing but is unable to complete all subsequent visits at the study site, as scheduled in Periods 3 and 4, for criteria other than those described for study discontinuation in Protocol Section 3.5. for study discontinuation, the participant they should be followed by telephone for up for 250 days after mAb infusion. During follow up with telephone check-ups, participants should be followed every 4 weeks to monitor for AEs and retrieve urine pregnancy results (kits to be provided at the last study site visit and a positive urine pregnancy result will require confirmation with a serum pregnancy test at the study site). At the end of all follow-up monitoring, participants will undergo the end-of-follow-up visit at the study site.

h Participants who restart ART in Period 4A will complete 6 study visits scheduled every 2 weeks over a 12-week period.

i Participants who opt to remain off ART and complete the ATI extension will complete 6 study visits scheduled every 2 weeks over a 12-week period.

j VES dose administration to occur at baseline/Day 0 and then every 2 weeks up to Dose 10.

k VRC07-523LS and CAP256V2LS sequential dose administration to occur only once at Day 7.

1.3. Sample Size and Power

The sample size in this study is determined based on practical considerations and empirical experience with similar types of studies. No sample size and power calculation were performed. Up to 25 participants will provide a preliminary assessment of descriptive safety, efficacy, and PK.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analyses

Prior to the final analysis, interim analyses may be conducted, and the analyses may be submitted to regulatory agencies to seek guidance for the overall clinical development program.

2.1.1. Planned Internal Analyses

Two interim internal analyses are planned to be conducted:

- After all participants have completed their Day 133 visit (last scheduled study visit of Period 2), started Period 4A (if the ART restart criteria are met), or prematurely discontinued the study
- After all participants have completed the end-of-Period 3 visit, or prematurely discontinued the study

2.1.2. Data Monitoring Committee Analysis

An external multidisciplinary Data Monitoring Committee (DMC) reviewed the progress of the study and performed interim reviews of the safety data of a sentinel cohort before opening enrollment of up to a further 20 participants, in order to protect participant welfare and preserve study integrity. To ensure the best interests of the participants, the DMC has made recommendations to the sponsor if the nature, frequency, and severity of adverse effects associated with the study treatment warrant the early termination of the study, the continuation of the study, or the continuation of the study with modifications.

The review was conducted after the 5 participants from the sentinel cohort had completed their Day 21 visit or had prematurely discontinued the study.

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

2.2. Final Analysis

The final analysis will be performed after all participants have completed the study or prematurely terminated from the study, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized.

2.3. Changes From Protocol-Specified Analyses

The second interim analysis was not performed as the last participant's completion of end-of-Period 3 visit occurred late to meet the CROI 2025 conference abstract submission deadline. To ensure timely abstract submission, an ad-hoc analysis was performed instead.

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. The treatment group to which participants were initially assigned will be used in the listings. 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 reason for their exclusion will be summarized.

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 who received a study participant identification number in the study after screening. This is the primary analysis set for by-participant listings.

3.1.2. Full Analysis Set

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

3.1.3. Safety Analysis Set

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

3.1.4. Pharmacokinetic Analysis Set

The VES PK Analysis Set includes all enrolled participants who took at least 1 dose of VES and have at least 1 non-missing postdose VES concentration value reported by the PK laboratory.

The VRC07-523LS PK Analysis Set includes all enrolled participants who took at least 1 dose of VRC07-523LS and have at least 1 non-missing postdose VRC07-523LS concentration value reported by the PK laboratory.

The CAP256V2LS PK Analysis Set includes all enrolled participants who took at least 1 dose of CAP256V2LS and have at least 1 non-missing postdose CAP256V2LS concentration value reported by the PK laboratory.

These are the primary analysis sets for all PK analyses.

3.1.5. Immunogenicity Analysis Set

The VRC07-523LS Immunogenicity Analysis Set includes all enrolled participants who took at least 1 dose of VRC07-523LS and have at least 1 non-missing postdose antidrug antibody (ADA) result for immunogenicity evaluation.

The CAP256V2LS Immunogenicity Analysis Set includes all enrolled participants who took at least 1 dose of CAP256V2LS and have at least 1 non-missing postdose ADA result for immunogenicity evaluation.

The VRC07-523LS and CAP256V2LS Immunogenicity Analysis Set includes all enrolled participants who took at least 1 dose of VRC07-523LS and 1 dose of CAP256V2LS and have at least 1 non-missing postdose ADA result for both immunogenicity evaluations.

3.2. Participant Grouping

For analyses based on All Enrolled Analysis Set and FAS, participants will be grouped according to the treatment to which they were enrolled (i.e., VES + VRC + CAP). For analyses based on Safety Analysis Set, PK Analysis Set and Immunogenicity Analysis Set, participants will be grouped according to the actual treatment received.

3.3. 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.

3.4. Examination of Participant Subgroups

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

3.5. Multiple Comparisons

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

3.6. Missing Data and Outliers

3.6.1. Missing Data

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

The handling of missing or incomplete dates for AE start is described in Section 7.1.6.2, and for prior and concomitant medications in Section 7.4.2. 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.

3.6.2. 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.

Individual study drug concentration values may be identified as outliers by the clinical pharmacokineticist and excluded from concentration summary tables and figures and from the noncompartmental PK analysis. Outlier drug concentrations will be identified in the concentration listing along with the justification for exclusion.

3.7. Data Handling Conventions and Transformations

Only year of birth is collected on the CRF; “01July” will be imputed as the day and month of birth.

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 (e.g., estimates of creatinine clearance, age at date of AE) will be based on age derived from date of birth and the date of the measurement or event, unless otherwise specified.

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

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

- The lower or ULOQ 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 limit of quantitation (LOQ), respectively).

If methods based on the assumption that the data are normally distributed are not adequate, analyses may be performed on transformed data or nonparametric analysis methods may be used, as appropriate.

Logarithmic (base 10) transformations will be applied to HIV-1 RNA data for efficacy analysis. For analysis purposes, HIV-1 RNA results of "<20 cp/mL" or not detectable will be imputed as 19 copies/mL, "<30 cp/mL" will be imputed as 29 copies/mL; "<100 cp/mL" will be imputed as 99 copies/mL.

Natural logarithm transformation will be used for analyzing not below the limit of quantitation (non-BLQ) concentrations and PK parameters in intensive PK samples. 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, first quartile [Q1], median, third quartile [Q3], and maximum) will be displayed as 0 and the rest of the summary statistics (i.e., standard deviation [SD] and coefficient of variation [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, 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:

- 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 plots, if more than one-third of the participants have concentration values of BLQ, then the mean and standard deviation are not displayed at that timepoint; and if more than one-half of the participants have concentration values of BLQ, then the median and quartiles are not displayed at that timepoint.

Concentration related PK parameters (e.g., C_{last}, C_{max}) that are BLQ will be excluded before log transformation or statistical model fitting and displayed as described above.

3.8. Visit Definitions

3.8.1. Definition of Key Dates and Study Day

Study Days are calculated from the first dosing date of study drug and derived as follows:

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

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

Baseline Value is defined as the last value obtained on or prior to the first dose of study drug.

Last Dose Date is defined as the latest dose date of any study drug as recorded on the Study Drug Administration eCRF (i.e., VES, VRC07-523LS, CAP256V2LS).

Last Study Date is the latest clinic visit date, and/or the laboratory visit dates, and/or latest AE onset date and end date, whichever is latest, including the any follow-up visit dates for participants who completed study.

Last Exposure Date is defined as last study date for all participants who receive VRC07-523LS and/or CAP256V2LS infusion. This date is defined considering the prolonged exposure of VRC07-523LS and CAP256V2LS after the last dose date through the end of study.

ATI Start Date is defined as the last stop date of Non-Study Antiretroviral (ARV) Medication between the study drug start and discontinuation, plus one day.

ART Restart Date is defined as the start date of resuming ART or compatible regimen after ATI start on Non-Study ARV Medication eCRF form.

3.8.2. Analysis Visits

The nominal visit as recorded on the eCRF or lab date 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 dose of study drug may be included in the calculation of baseline value, if applicable.
- Unscheduled visits after the first dose of study drug will be included in determining the maximum postbaseline toxicity grade and time to event analyses.
- For participants who prematurely discontinued from the study drug, early termination (ET) data will be summarized as a separate visit, labeled as “Early Study Drug Discontinuation”.
- Data obtained after the follow-up visit or last exposure date (whichever is later) will be excluded from the summaries but will be included in the listings.

3.8.3. Selection of Data in the Event of Multiple Records for a Visit

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

If multiple valid, non-missing, numeric measurements exist on the same nominal visit, records will be chosen based on the following rules if a single value is needed:

- In general, the baseline value will be the last non-missing value on or prior to the first dosing date of study drug, unless specified differently. If multiple measurements occur on the same day, the last non-missing value prior to the time of first dosing of study drug will be considered as the baseline value. If these multiple measurements occur at the same time or the time is not available, the average (geometric mean for HIV-1 RNA and arithmetic mean for others) of these measurements will be considered as the baseline value.

- For postbaseline visits, the value for the scheduled visit only will be used. If there is more than one record on the selected visit, the average will be taken (geometric mean for HIV-1 RNA and arithmetic mean for others), unless otherwise specified.

If multiple valid, non-missing, categorical measurements exist on the same nominal visit, records will be chosen based on the following rule if a single value is needed:

- For baseline, the last available record on or prior to the first dose 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 (e.g., normal will be selected over abnormal for safety ECG findings).

- For postbaseline visits, the value for the scheduled visit only will be used. If multiple records are available for a scheduled visit, the most conservative value within that visit will be selected (e.g., abnormal will be selected over normal for safety ECGs).

4. SUBJECT DISPOSITION

4.1. Participant Enrollment and Disposition

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

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

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

- 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. 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:

- Reasons for premature study drug or study discontinuation

4.2. Extent of Study Drug Exposure

A participant's extent of exposure to study drug will be generated from the study drug administration data. Exposure data will be summarized.

4.2.1. Duration of Exposure to Study Drug

Duration of exposure to study drug will be defined as the last exposure date minus the first dose date plus 1, regardless of any temporary interruptions in study drug administration, and will be expressed in weeks using up to 1 decimal place (e.g., 4.5 weeks).

Duration of exposure will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) and as the number (i.e., cumulative counts) and percentage of participants exposed through the following periods: 1 day, 2 weeks, 4 weeks, 6 weeks, 8 weeks, 10 weeks, 12 weeks, 14 weeks, 16 weeks, 18 weeks, 20 weeks, 34 weeks, 48 weeks, and 59 weeks.

Summaries will be provided for the Safety Analysis Set.

Dosing information for individual participants will be listed.

4.2.2. Study Drug Administration for VES

Study drug administration for VES for participants in the Safety Analysis Set will be summarized for the following items:

- Number and percentage of participants who received at least 3 VES doses, 4 VES doses, 5 VES doses, 6 VES doses, 7 VES doses, 8 VES doses, 9 VES doses, and 10 VES doses.
- Number and percentage of participants who received 6 mg VES on 1st dose
- Number and percentage of participants who received 6 mg VES on 2nd dose
- Number and percentage of participants who received 6 mg VES on 3rd dose
- Number and percentage of participants who received 8 mg VES on 3rd dose
- Number and percentage of participants who received 8 mg VES on 4th dose and onwards

4.2.3. Study Drug Administration for VRC07-523LS and CAP256V2LS

Study drug administration for participants in the Safety Analysis Set will be summarized for the following items:

- Number and percentage of participants who received IV infusion of VRC07-523LS on Day 7.
- Number and percentage of participants who received IV infusion of CAP256V2LS on Day 7.

4.3. Protocol Deviations

Participants who did not meet the eligibility criteria for study entry but enrolled in the study, will be summarized regardless of whether they were exempted by the sponsor or not. 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 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 for the All Enrolled Analysis Set. Additionally, the number and percentage of participants with at least 1, 1, 2, or 3 or more important protocol deviations will be summarized. 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 specifying whether the protocol deviation is important.

4.4. Assessment of Disaster or Public Health Emergency Impact

This study was ongoing during the novel coronavirus (COVID-19) pandemic which had an impact on the study conduct. Some participants may have been unable to attend onsite visits due to shelter in place guidelines, site closures, or other reasons. This section describes how special situations due to COVID-19 will be handled in the analysis. Please refer to Appendix 2 for data collection and determination of COVID-19 impact Data.

4.4.1. Study Drug or Study Discontinuation Due to Disaster or Public Health Emergency

A by-participant listing of reasons for premature study drug or study discontinuation due to COVID-19 will be provided if applicable.

4.4.2. Protocol Deviations Due to Disaster or Public Health Emergency

A by-participant listing will be provided for participants with protocol deviations related to COVID-19 if applicable.

4.4.3. Missed and Virtual Visits due to Disaster or Public Health Emergency

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

Information regarding missed or virtual visits due to COVID-19 will be collected as free text in the CRF comment fields. The determination of missed or virtual visits due to COVID-19 will be done using Natural Language Processing (NLP) to search the CRF comment fields. A detailed explanation of the algorithm is given in Appendix 2.

4.4.4. Adverse Events Due to Disaster or Public Health Emergency

AEs of COVID-19 will be included in analyses of AEs if applicable, which will be determined through COVID-19 SMQ Narrow search. A by-participant listing of AEs of COVID-19 will be provided if applicable.

5. BASELINE CHARACTERISTICS

5.1. Demographics and Baseline Characteristics

Participant demographic variables (i.e., age, sex, race, and ethnicity) and baseline characteristics (body weight [in kg], height [in cm], body mass index [BMI; in kg/m^2]) will be summarized 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.

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

Other baseline characteristics will be summarized:

- Baseline HIV-1 RNA ($\log_{10}$ copies/mL)
- Baseline HIV-1 RNA categories (copies/mL) (a) < 50 and (b) ≥ 50
- Baseline CD4+ T cell count (cells/µL)
- Baseline CD4+ T cell count categories (cells/µL): (a) < 50, (b) ≥ 50 to < 200, (c) ≥ 200 to < 350, (d) ≥ 350 to < 500, and (e) ≥ 500
- Baseline CD4+ T cell percentage (%)
- Baseline estimated glomerular filtration rate using Cockcroft-Gault formula $eGFR_{CG}$ (mL/min)
- HIV disease status
- Mode of infection (HIV risk factors)
- Time from HIV diagnosis to ART initiation (in days)
- Duration of ART prior to study (in years)
- Fiebig Stage at ART Initiation
- CD4+ T cell count prior to start of initial ART (cells/µL)
- CD4+ T cell count categories prior to start of initial ART (cells/µL): (a) < 50, (b) ≥ 50 to < 200, (c) ≥ 200 to < 350, (d) ≥ 350 to < 500, and (e) ≥ 500

- HIV-1 RNA at HIV diagnosis ($\log_{10}$ copies/mL)
- HIV-1 RNA categories at HIV diagnosis (copies/mL) (a) ≥ 50 to < 2000, (b) ≥ 2000 to ≤ 5000, (c) > 5000
- HIV-1 RNA prior to start of initial ART ($\log_{10}$ copies/mL)
- HIV-1 RNA categories prior to start of initial ART (copies/mL): (a) ≥ 50 to < 2000, (b) ≥ 2000 to ≤ 5000, (c) > 5000

These baseline characteristics will be summarized using descriptive statistics for continuous variables 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

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

6. EFFICACY ANALYSES

6.1. Definition of Efficacy Endpoints

Efficacy endpoints include the following:

- Time to virologic rebound following ATI based on 2 different cutoff values:
  1) ≥ 50 copies/mL
  2) ≥ 200 copies/mL
- Change in plasma viral load set-point following ATI
- Time to ART resumption following ATI

6.2. Statistical Hypotheses for Efficacy Endpoints

CCI [redacted]

6.3. Analysis of Efficacy Endpoints

The Full Analysis Set will be used for the efficacy endpoint analysis.

Descriptive statistics will be provided for HIV-1 RNA data as follows:

- Baseline HIV-1 RNA value
- Change from baseline in HIV-1 RNA ($\log_{10}$ copies) at each postbaseline visit up to the last exposure date for participants who have permanently discontinued study drug.

The baseline HIV-1 RNA 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, and summarized using descriptive statistics (n, mean, SD, 95% confidence interval [CI], median, Q1, Q3, minimum, and maximum). The mean, median, Q1, Q3, minimum, and maximum values will be displayed to the reported number of digits; SD values will be displayed to the reported number of digits plus 1. In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.8.3. No formal statistical testing is planned.

The change in plasma viral load set-point is defined as the value following ATI minus the pre-ART value. The plasma viral set-point following ATI is calculated as the geometric mean of all the HIV-1 RNA measurements between a specified start and end date. The start date and end date will be provided by the study's clinical development team and clinical virologist based on individual participant data review. The pre-ART set point value is the HIV-RNA load count prior to start of initial ARV treatment recorded in the clinical database. Change in plasma viral load set-point following ATI will be summarized and analyzed in the same fashion as that of the change from baseline in plasma $\log_{10}$ HIV-1 RNA.

A by-participant listing for HIV-1 RNA value will be provided by participant ID number and visit in chronological order.

A figure of individual participant $\log_{10}$ HIV-1 RNA value versus time following ATI will be provided.

Virologic rebound is defined as: at any visit a rebound in HIV-1 RNA to cutoff value, which is subsequently confirmed at the following scheduled or unscheduled visit.

Time to virologic rebound will be analyzed using the Kaplan-Meier method. Participants who do not rebound will be censored at the last HIV-1 RNA collection date during ATI period.

Time to ART resumption following ATI will be analyzed in the same fashion as that of the time to virologic rebound using the Kaplan-Meier method. Participants who do not resume ART will be censored at the last study date. Participants with ART resumed on or prior to end of Period 3 visit date will be flagged.

The above time-to-event endpoints are defined as the time interval (in weeks) between the ATI start date and the event or censoring date, calculated as (the event or censoring date – ATI start date + 1) / 7.

7. SAFETY ANALYSES

Analysis of safety data will be conducted on the Safety Analysis Set, unless otherwise specified in the following sections. The treatment-emergent (TE) period is defined as the time period from the first dose date of study treatment up to and including last exposure date after permanent discontinuation of study drug.

7.1. Adverse Events and Deaths

7.1.1. Adverse Event Dictionary

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

7.1.2. Adverse Event Severity

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

7.1.3. Relationship of Adverse Events to Study Drug

Related AEs are those for which the investigator selected "Related" on the AE eCRF 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.

7.1.4. Relationship of Adverse Events to Study Procedure

Study procedure related AEs are those for which the investigator selected "Yes" on the AE eCRF 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 shown as missing from that captured on the eCRF in by-participant data listings.

7.1.5. Serious Adverse Events

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

7.1.6. Treatment-Emergent Adverse Events

7.1.6.1. Definition of Treatment-Emergent Adverse Events

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

- Any AEs that start during the TE period.
- Any AEs leading to premature discontinuation of study drug.

7.1.6.2. 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 TE. The event is considered TE 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 last day of the TE period

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 to be TE. 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 TE.

7.1.7. Summaries of Adverse Events and Deaths

TEAEs will be summarized based on the Safety Analysis Set.

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

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

- TEAEs

For the AE categories described below, summaries will be provided by SOC and PT:

- TEAEs by severity
- TEAEs with Grade 3 or higher
- TEAEs with Grade 2 or higher

- TE treatment-related AEs
- TE VES-related AEs
- TE VRC07-523LS-related AEs
- TE CAP256V2LS-related AEs
- TE treatment-related AEs with Grade 3 or higher
- TE treatment-related AEs with Grade 2 or higher
- TE SAEs
- TE treatment-related SAEs
- TEAEs leading to death (i.e., Grade 5 AEs)
- TEAEs leading to premature discontinuation of any 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, Grade 3 or Higher TEAEs, TE SAEs, TE treatment-related AEs, Grade 3 or Higher TE treatment-related AEs, Grade 2 or Higher 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, including whether the event is TE
- All SAEs
- All Deaths
- All AEs leading to premature discontinuation of any study drug

7.1.8. Additional Analysis of Adverse Events

The following categories of TEAEs of interest will be summarized:

- Infusion related reactions, as defined per eCRF (i.e., AE with "Yes" answer to "Is this part of an infusion-related reaction?" in AE eCRF). The denominator for the percentage calculation will be based on the number of participants who received at least one infusion in the Safety Analysis Set.

- Potential Cytokine Release Syndrome (CRS) and Flu-like AEs, utilizing a MedDRA search term (MST) list "Cytokine Release Syndrome - HIV Cure therapy" developed by Gilead. The denominator for the percentage calculation will be based on the number of participants in the Safety Analysis Set.

For each AE of interest category, the number and percentage of participants who experienced any of the above events will be summarized by SOC, PT and severity. AEs of each interest category will be summarized by PT only, in descending order of total frequency. The number and percentage of participants who experienced treatment related potentially CRS and flu-like AEs will be summarized by PT and by SOC, PT and severity. In addition, the number and percentage of participants who experienced treatment related potentially CRS and flu-like AEs will be summarized separately by PT for VES-related, VRC07-523LS-related, and CAP256V2LS-related events. Data listings will be provided for each AE of interest category.

7.2. 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 in TE period defined at the beginning of Section 7. 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. Values falling outside of the relevant reference range and/or having a severity grade of 1 or higher will be flagged in the data listings, as appropriate.

No formal statistical testing is planned.

7.2.1. Summaries of Numeric Laboratory Results

Descriptive statistics will be provided for each laboratory test specified in the study protocol as follows, as appropriate:

- Baseline values

- Values at each postbaseline visit

- Change from baseline at each postbaseline visit

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.

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

7.2.2. Graded Laboratory Values

The Gilead Grading Scale for Severity of Adverse Events and Laboratory Abnormalities, Antiviral Toxicity Grade Scale, Version 01 April 2015 will be used to assign toxicity grades (0 to 5) to laboratory results for analysis. Grade 0 includes all values that do not meet the criteria for an abnormality of at least Grade 1. For laboratory tests with criteria for both increased and decreased levels, analyses for each direction (i.e., increased, decreased) will be presented separately.

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

7.2.2.1. Treatment-Emergent Laboratory Abnormalities

Treatment-emergent laboratory abnormalities (TELAs) are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point during the TE period defined at the beginning of Section 7. If the relevant baseline laboratory value is missing, any abnormality of at least Grade 1 observed within the time frame specified above will be considered treatment emergent.

7.2.2.2. Summaries of Laboratory Abnormalities

Laboratory data that are categorical will be summarized using the number and percentage of participants in the study with the given response at baseline and each scheduled postbaseline visit.

The following summaries (number and percentage of participants) for TELAs will be provided by lab test; participants will be categorized according to the most severe postbaseline abnormality grade for a given lab test:

- Graded laboratory abnormalities
- Grade 3 or 4 laboratory abnormalities

For all summaries of laboratory abnormalities, the denominator is the number of participants with non-missing postbaseline values during the TE period defined at the beginning of Section 7.

A by-participant listing of TE 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 and abnormal flags displayed.

7.3. Body Weight and Vital Signs

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

- Baseline value
- Values at each postbaseline visit and time point
- Change from baseline at each postbaseline visit and time point

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 and time point will be defined as the postbaseline value minus the baseline value.

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.8.3. At each visit, the body weight recorded repeatedly on multiple timepoints will be collapsed into one record. No formal statistical testing is planned.

A by-participant listing of vital signs will be provided by participant ID number and time point 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.

7.4. Prior and Concomitant Medications

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

7.4.1. Nonstudy Drug Antiretroviral Medications

Any nonstudy drug ARV medications used prior to, during, or after the study (if collected) are all recorded on the ARV eCRF. The WHO preferred name and drug code will be attached to the clinical database. All nonstudy drug ARV medications recorded on the ARV eCRF will be listed. No inferential statistics will be provided.

7.4.2. Concomitant Non-Antiretroviral Medications

Concomitant non-ARV medications (i.e., non-ARV medications other than study drug that are taken while receiving study drug) will be coded using the WHO Drug Dictionary. The WHO preferred name and drug code will be attached to the clinical database. Use of concomitant medications from the first dose date of study drug up to the last day of TE period will be summarized (number and percentage of participants)by WHO drug class and preferred name. Multiple drug use (by preferred name) will be counted only once per participant. The summary will be sorted alphabetically by drug class and then by decreasing total frequency within a class.

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

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

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

Summaries of non-ARV concomitant medications will be based on the Safety Analysis Set. No formal statistical testing is planned. A by-participant listing for all non-ARV concomitant medications will be listed and sorted by participant ID number and administration date in chronological order.

7.5. Electrocardiogram Results

The investigator's assessment of ECG results (normal; abnormal; not clinically significant; abnormal, clinically significant) are collected at screening, end of period 3 visit for participants who have completed Period 3 or meet the ART restart criteria, and end of study visit for participants who have completed Period 4A or 4B. A by-participant listing for ECG assessment results will be provided by participant ID number.

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

8.1. PK Sample Collection and Concentration

PK concentration data from plasma PK samples of VES and serum PK samples of VRC07-523LS and CAP256V2LS collected at the timepoints stated in Appendix 1 will be listed and summarized using the PK analysis set. PK concentration data from plasma PK samples of dolutegravir will be listed using the All Enrolled Analysis Set.

8.1.1. Estimation of PK Parameters

PK parameters will be estimated using Phoenix WinNonlin® software using standard noncompartmental methods. The linear up/log down rule will be used in conjunction with the appropriate noncompartmental model, with input values for dose level, dosing time, plasma concentration, and corresponding real-time values, based on drug dosing times whenever possible.

All predose sample times before time-zero will be converted to zero.

For area under the curve (AUC), samples BLQ of the bioanalytical assays occurring prior to the achievement of the first quantifiable concentration will be assigned a concentration value of zero to prevent overestimation of the initial AUC. Samples that are BLQ at all other time points will be treated as missing data in WinNonlin. The nominal time point for a key event or dosing interval (τ) may be used to permit direct calculation of AUC over specific time intervals. The appropriateness of this approach will be assessed by the PK scientist on a profile-by-profile basis.

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

8.1.2. PK Parameters

The analytes and parameters presented in Table 8-1 will be used to evaluate the PK objectives of the study. The PK parameters to be estimated in this study are listed and defined in the PK Abbreviations section.

Table 8-1. PK Parameters for VES

Analyte	Parameters
VES	AUC_{inf}, AUC_{last}, AUC_{exp}, C_{max}, T_{max}, C_{last}, T_{last}, $t_{1/2}$, CL/F, and V_z/F
VRC07-523LS	AUC_{inf}, AUC_{last}, AUC_{exp}, C_{max}, T_{max}, C_{last}, T_{last}, $t_{1/2}$, CL, V_{ss}, and V_z
CAP256V2LS	AUC_{inf}, AUC_{last}, AUC_{exp}, C_{max}, T_{max}, C_{last}, T_{last}, $t_{1/2}$, CL, V_{ss}, and V_z

8.1.3. Statistical Analysis Methods

Individual participant concentration data and individual participant PK parameters for VES, VRC07-523LS, and CAP256V2LS will be listed and summarized using descriptive statistics for participants in the corresponding analyte PK analysis set. Summary statistics (number of participants, mean, SD, CV, median, min, max, Q1, and Q3) will be presented for both individual participant concentration data by time point and individual participant PK parameters. For individual participant concentration data for VRC07-523LS and CAP256V2LS, the summaries will only be presented through end of Period 3, since the actual time from study drug dosing varies depending on the time of ART restart for visits after end of Period 3 visit. Moreover, the geometric mean, geometric mean coefficient of variation (GCV), 95% CI for the geometric mean, and the mean and SD of the natural log-transformed values will be presented for individual participant PK parameter data.

Individual concentration data listings and summaries will include all participants with concentration data. If a participant has quantifiable pre-dose, BLQ at end of infusion, or received an incorrect dose, the related PK concentration(s) will be included in the table but will be excluded from the summary statistics, with reasons for exclusion identified. The sample size for each time point will be based on the number of participants with non-missing concentration data at that time point. The number and percentage of participants with concentration BLQ, as well as an indicator if more than one-third of the participants have concentration BLQ, will be presented for each time point. For summary statistics, BLQ values will be treated as zero at baseline and postdose time points. The method to handle BLQ values for PK summaries are described in Section 3.7. Concentration values will be presented as received from the bioanalytical lab and summary statistics will be presented to three significant digits.

Individual PK parameter data listings and summaries will include all participants for whom PK parameter(s) can be derived. The sample size for each PK parameter will be based on the number of participants with non-missing data for that PK parameter. PK parameters could be unestimatable due to insufficient concentration data or may be estimated but marked for exclusion due to reasons such as the participant received an incorrect dose. In such cases, the PK parameters will be included in the table but will be excluded from the summary statistics, with reasons for exclusion identified.

The following tables will be provided for each analyte:

- Individual participant concentration data and summary statistics
- Individual participant plasma/serum PK parameters and summary statistics

The following figures may be provided for each analyte:

- Mean (± SD) concentration data versus time (on linear and semilogarithmic scales)
- Median (Q1, Q3) concentration data versus time (on linear and semilogarithmic scales)

- Individual participant plasma/serum concentrations versus time (on linear and semilogarithmic scales)

Individual, mean, and median postdose concentration values that are BLQ will not be displayed in the figures and the remaining points will be connected.

PK sampling details by participant, including differences in scheduled and actual collection times and sample age, will be provided in listings. In addition, determination of half-life and corresponding correlation coefficient will be listed.

8.2. Changes From Protocol-Specified PK Analyses

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

9. IMMUNOGENICITY ANALYSES

9.1. Definition of Terminology

Participants Evaluable for ADA Prevalence: participants who have at least one reportable ADA result at baseline or post-baseline.

Participants Evaluable for ADA Incidence: participants who have at least one reportable ADA result at post-baseline.

ADA Prevalence: the proportion of participants who have at least one positive ADA sample (baseline or post-baseline) among all participants evaluable for ADA prevalence.

ADA Incidence: the proportion of participants who have treatment-emergent ADA among all participants evaluable for ADA incidence.

Treatment-Emergent ADA: either treatment-boosted or treatment-induced ADA.

Treatment-Boosted ADA: defined as positive baseline ADA sample and at least one positive post-baseline ADA sample and (the max titer of the post-baseline ADA) / (titer of baseline ADA) ≥ 4. Also, if baseline is positive and titer is less then limit of detection and post-baseline titer is equal to or greater than limit of detection, it is considered treatment-boosted. The proportion of participants who have treatment-boosted ADA is calculated based on the total number of participants evaluable for ADA incidence as the denominator.

Treatment-Induced ADA: defined as negative or missing baseline ADA sample and at least one positive post-baseline ADA sample. The proportion of participants who have treatment-induced ADA is calculated based on the total number of participants evaluable for ADA incidence as the denominator.

Persistent ADA: defined as a) treatment-induced ADA detected at two or more sampling time points during the study, where the first and last ADA-positive sample (irrespective of any negative samples in between) are separated by a period of 16 weeks or longer; or b) treatment-induced ADA detected at the last sampling time point of the study. The proportion of participants who have persistent ADA is based on the total number of participants evaluable for ADA incidence as the denominator.

Transient ADA: defined as treatment-induced ADA that does not meet the definition of persistent ADA. The proportion of participants who have transient ADA is based on the total number of participants evaluable for ADA incidence as the denominator.

Participant-level ADA status: defined as “ADA+” if the participant has treatment- emergent ADA; “ADA-” if the participant is evaluable for ADA incidence and does not have treatment-emergent ADA; missing if the participant is not evaluable for ADA incidence.

Time to ADA onset: for participants with treatment-induced ADA, defined as the number of days after first dose to the day when the first positive ADA result was detected; for participants with treatment-boosted ADA, defined as the number of days after first dose to the day when the first boosted post-baseline positive ADA result was detected. A post-baseline positive ADA result is boosted if (titer of the post-baseline ADA) / (titer of baseline ADA) ≥ 4.

9.2. Evaluation of Immunogenicity Data

Based on the respective evaluable populations, the following measures of immunogenicity will be reported: ADA prevalence, ADA incidence, and Transient/Persistent ADA.

The numbers and percentages of participants within each ADA category described above will be summarized over the entire study period. In addition, the number and percentage of positive and negative ADA samples will be summarized by visit. ADA titer values in positive ADA samples will be summarized (including median, Q1, Q3, minimum and maximum titer values) by visit. Time to ADA onset in ADA+ participants will also be summarized (including median, Q1, Q3, minimum and maximum onset times).

The ADA summary tables will be generated for (1) anti-VRC07-523LS, (2) anti-CAP256V2LS, and (3) both anti-VRC07-523LS and anti-CAP256V2LS.

By-participant listing of ADA result, titer, and corresponding PK concentration by participant ID number and visit, as well as participant-level ADA status, ADA type (persistent or transient), and time to ADA onset will be provided for all participants in the Immunogenicity Analysis Set. A separate listing will be produced for participants with any positive ADA results. The ADA titer values in ADA+ participants will be plotted over time by individual participant. For the purpose of plotting, samples with negative ADA result or undetectable titer will have the titer value imputed to zero and connected with the adjacent time points.

In order to evaluate the impact of ADA on PK, combined individual PK concentration-time profile plots will be produced with ADA+ participants highlighted in red. Plots of individual ADA titer values in ADA+ participants over time will be produced. ADA titer values less than the minimum reportable titer value and titer values for ADA-negative samples will be imputed to 0.

10. SOFTWARE

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

Phoenix WinNonlin® 8.0 Certara USA, Inc., Radnor, PA, USA.

11. SAP REVISION

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

12. APPENDICES

Appendix 1. Schedule of Assessments

			P1									P2[a]																P3[a,b]		P4[a,b]		
Visit[c]	**Screening[d]**	**Day –13/Prebaseline**	**VES Dose1-Day 0/Baseline**	**Day 1**	**Day 2**	**VRC & CAP Dose–Day 7**	**Day 8**	**Day 9**	**VES Dose 2-Day 14**	**Day 21**	**VES Dose 3-Day 28[e]**	**Day 35**	**VES Dose 4-Day 42**	**Day 49**	**VES Dose 5-Day 56**	**Day 57**	**Day 63**	**VES Dose 6-Day 70**	**Day 77**	**VES Dose 7-Day 84**	**Day 91**	**VES Dose 8-Day 98**	**Day 105**	**VES Dose 9-Day 112**	**Day 119**	**VES Dose 10-Day 126**	**Day 127**	**Day 128**	**Day 133**	**Day 134-336**	**End-of-Period 3 Visit[f]**	**Day 337-413**	**End-of-Study Visit[g]**	**ESDD[h]**
Informed consent	X																																
Medical history	X[i]	X																															
AE and Con Med	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Complete physical exam	X																																
Symptom-directed physical exam		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[j]	X	X[k]	X	X
12-Lead ECG	X																													X		X	
Vital signs[l]	X		X	X		X			X		X		X		X			X		X		X		X		X				X[j]	X	X[k]	X	X
Body weight	X	X	X	X	X	X	X	X	X	X	X		X		X			X		X		X		X		X				X[j]	X	X[k]	X	X
Height	X																																
Review of I/E criteria		X																															
Urinalysis	X	X	X	X	X	X			X	X	X		X		X			X		X		X		X		X			X	X[j]		X[k]	X	X
Urine pregnancy test[m]		X	X								X		X					X				X				X				X[j]		X[k]	X	X
Chemistry[n]	X	X	X[o]	X	X	X			X	X	X		X		X			X		X		X		X		X				X[j]		X[k]	X	X
Hematologyp	X	X	X[o]	X	X	X			X	X	X		X		X			X		X		X		X		X				X[j]		X[k]	X	X
Metabolic assessmentq	X																																

			P1									P2[a]																	P3[a,b]		P4[a,b]		
Visit[c]	**Screening[d]**	**Day –13/Prebaseline**	**VES Dose1-Day 0/Baseline**	**Day 1**	**Day 2**	**VRC & CAP Dose–Day 7**	**Day 8**	**Day 9**	**VES Dose 2-Day 14**	**Day 21**	**VES Dose 3-Day 28[e]**	**Day 35**	**VES Dose 4-Day 42**	**Day 49**	**VES Dose 5-Day 56**	**Day 57**	**Day 63**	**VES Dose 6-Day 70**	**Day 77**	**VES Dose 7-Day 84**	**Day 91**	**VES Dose 8-Day 98**	**Day 105**	**VES Dose 9-Day 112**	**Day 119**	**VES Dose 10-Day 126**	**Day 127**	**Day 128**	**Day 133**	**Day 134-336**	**End-of-Period 3 Visit[f]**	**Day 337-413**	**End-of-Study Visit[g]**	**ESDD[h]**
Creatinine clearancer	X	X	X	X	X	X			X	X	X		X		X			X		X		X		X		X			X[j]		X[k]	X	X
Follicle-stimulating hormones	X																																
Whole blood ISG mRNA panel		X	X[o]	X											X	X										X	X			X		X	X
HIV-specific antibody profiling using plasma		X	X[o]				X																			X			X		X		X	
HIV staging[ff]	X																																
Serum pregnancy testm	X																																
CD4+ and CD8+ T cell absolute count, percentage, and CD4/CD8 ratio	X		X[o]						X		X		X		X			X		X		X		X		X			X[j]	X	X[k]	X	X
HBV/HCV serologyt	X																																
VES PKu			X	X	X																												
Serum VRC07-523LS & CAP256V2LS PKv						X	X	X	X	X	X				X					X				X				X	X		X			
Plasma dolutegravir PKw															X					X				X				X	X		X			
Plasma HIV-1 RNAx	X	X	X[o]			X			X	X	X		X		X			X		X		X		X		X			X	X	X	X	X	X
Plasma HIV-1 resistance testing to VRC07-523LS, CAP256V2LS, and baseline ART			X[o]			X			X	X	X		X		X			X		X		X		X		X			X	X	X	X	X	X
Plasma for active HIV 1 reservoir		X	X[o]	X	X										X	X										X	X	X			X		X	

			P1									P2[a]																P3[a,b]		P4[a,b]		
Visit[c]	**Screening[d]**	**Day –13/Prebaseline**	**VES Dose1-Day 0/Baseline**	**Day 1**	**Day 2**	**VRC & CAP Dose–Day 7**	**Day 8**	**Day 9**	**VES Dose 2-Day 14**	**Day 21**	**VES Dose 3-Day 28[e]**	**Day 35**	**VES Dose 4-Day 42**	**Day 49**	**VES Dose 5-Day 56**	**Day 57**	**Day 63**	**VES Dose 6-Day 70**	**Day 77**	**VES Dose 7-Day 84**	**Day 91**	**VES Dose 8-Day 98**	**Day 105**	**VES Dose 9-Day 112**	**Day 119**	**VES Dose 10-Day 126**	**Day 127**	**Day 128**	**Day 133**	**Day 134-336**	**End-of-Period 3 Visit[f]**	**Day 337-413**	**End-of-Study Visit[g]**	**FSDD[h]**
Soluble proteins in the TruCulture® Whole Blood Culture System		X																														
Soluble proteins (cytokines, chemokines, and inflammatory markers)		X	X[o]	X			X								X	X	X									X	X			X		X	X
PBMC sample for testing of viral sensitivity to the VRC07-523LS and CAP256V2LS mAbs	X[y]																												X[z]	X		X	
PBMC HIV-specific T cell responses		X					X										X											X		X		X	
PBMC immune cell frequency, activation, and phenotyping		X	X[o]	X			X								X	X	X									X	X			X		X	
PBMC latent HIV-1 reservoir		X																											X[z]	X		X	
PBMC active HIV-1 reservoir		X	X[o]	X	X										X	X										X	X	X		X		X	

			P1									P2[a]																P3 [a,b]		P4 [a,b]		
Visit[c]	**Screening[d]**	**Day −13/Prebaseline**	**VES Dose1-Day 0/Baseline**	**Day 1**	**Day 2**	**VRC & CAP Dose–Day 7**	**Day 8**	**Day 9**	**VES Dose 2-Day 14**	**Day 21**	**VES Dose 3-Day 28[e]**	**Day 35**	**VES Dose 4-Day 42**	**Day 49**	**VES Dose 5-Day 56**	**Day 57**	**Day 63**	**VES Dose 6-Day 70**	**Day 77**	**VES Dose 7-Day 84**	**Day 91**	**VES Dose 8-Day 98**	**Day 105**	**VES Dose 9-Day 112**	**Day 119**	**VES Dose 10-Day 126**	**Day 127**	**Day 128**	**Day 133**	**Day 134-336**	**End-of-Period 3 Visit[f]**	**Day 337-413**	**End-of-Study Visit[g]**	**ESDD[h]**
Anti-VRC07-523LS and anti-CAP256V2LS antibody profiling from serumaa		X									X				X					X				X				X	X[bb]		X[cc]		
Review of ongoing eligibility check prior to study dosing			X			X			X		X		X		X			X		X		X		X		X							
Birth control check		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X		
Participant agreement to follow study contraceptive requirements	X																																
In-clinic dosing			X			X			X		X[gg]		X[hh]		X[hh]			X[hh]		X[hh]		X[hh]		X[hh]		X[hh]							
VES dose			X						X		X		X		X			X		X		X		X		X							
VRC07-523LS and CAP256V2LS dose						X																											
CCI																																	
HLA genotype, TLR7, FcgR SNP		X																															
CCI																																	
HIV-1 reservoir measurement		X																											X[ee]	X		X	
Gene expression		X																											X[ee]	X		X	
HIV-specific T cell responses		X																											X[ee]	X		X	

			P1									P2[a]																P3 [a,b]		P4 [a,b]		
Visit[c]	**Screening[d]**	**Day −13/Prebaseline**	**VES Dose1-Day 0/Baseline**	**Day 1**	**Day 2**	**VRC & CAP Dose–Day 7**	**Day 8**	**Day 9**	**VES Dose 2-Day 14**	**Day 21**	**VES Dose 3-Day 28[e]**	**Day 35**	**VES Dose 4-Day 42**	**Day 49**	**VES Dose 5-Day 56**	**Day 57**	**Day 63**	**VES Dose 6-Day 70**	**Day 77**	**VES Dose 7-Day 84**	**Day 91**	**VES Dose 8-Day 98**	**Day 105**	**VES Dose 9-Day 112**	**Day 119**	**VES Dose 10-Day 126**	**Day 127**	**Day 128**	**Day 133**	**Day 134-336**	**End-of-Period 3 Visit[f]**	**Day 337-413**	**End-of-Study Visit[g]**	**ESDD[h]**
Immune cell frequency, activation and phenotyping		X																											X[ee]	X		X	

ESDD = early study drug discontinuation; GALT = gut-associated lymphoid tissue; HBV = hepatitis B virus; HCV = hepatitis C virus; HLA = human leucocyte antigen; I/E = inclusion/exclusion; ISG = interferon-stimulated gene; mAb = monoclonal antibody; mRNA = messenger RNA; P1/2/3/4 = Period ½/3/4; PBMC = peripheral blood mononuclear cell; PK = pharmacokinetic(s); PrEP = preexposure prophylaxis; SNP = single nucleotide polymorphism; TLR = toll-like receptor; VES = vesatolimod; VRC = VRC07-523LS

a Known HIV-1 seronegative sexual partners of enrolled study participants may be referred for HIV PrEP to decrease risk of HIV transmission during ATI in Periods 2, 3, and 4B.

b Periods 3 and 4 have study visit every 2 weeks.

c All study visits are to be completed within ± 3 days of the protocol-specified visit date (except end-of-Period 3 visit, which is ± 1 day). This tolerance window does not apply to screening, pre-baseline, Day 0, and Day 7.

d Evaluations to be completed within 35 days prior to prebaseline/Day −13.

e At the Day 28 visit and prior to the Period 2 Day 35 visit, participants will be assessed to determine whether the criteria necessary to begin ATI are met. All of the following criteria must be met for a participant to begin ATI: Viral load < 50 copies/mL; CD4+ T cell count > 400 cells/µL; negative urine pregnancy test; participant has received VRC07-523LS, CAP256V2LS, and at least 3 of the 10 scheduled doses of VES. Participant confirms agreement to request their partners to use condoms throughout the ATI period. The initiation of ATI (Period 2) may be postponed for up to 4 weeks after the last VES dose for participants to meet these requirements.

f Participants who complete Period 3 or meet the ART restart criteria will be required to complete an end-of-Period 3 visit 1 week after their last visit.

g End-of-study visit will occur 7 days (± 3 days) after completion of the final Period 4 visit.

h ESDD visit is required for participants who prematurely discontinue study drug prior to completing the infusions of the VRC07-523LS and CAP256V2LS, or all 10 doses of VES, as described in Protocol Section 6.9.1, will complete an ESDD visit within 3 days of informing the investigator/site.

i Medical history including route and estimated duration of HIV-1 infection, history of HIV-1 disease-related events, ART history for at least 12 consecutive months prior to screening, and prior concomitant medications within 35 days of the screening visit.

j Day 147 and at each visit every 4 weeks thereafter

k Day 343 and at each visit every 4 weeks thereafter

l Vital signs (blood pressure, pulse, respiration rate, oxygen saturation, and temperature) will be monitored on dosing days at the following time points: (1) VES Dose 1 on baseline/Day 0, at predose, then at 1, 2, 4, 8, 12, 18, and 24 hours (Day 1) postdose (2) VRC07-523LS and CAP256V2LS infusion, and remaining VES Doses 2 to 10 at predose, then at 1, 2, 4, and 8 hours postdose.

m Females of childbearing potential only. Positive urine pregnancy tests will be confirmed with a serum test.

n Alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, total bilirubin, direct and indirect bilirubin, total protein, albumin, creatine kinase, bicarbonate, blood urea nitrogen, calcium, chloride, creatinine, glucose, phosphorus, magnesium, potassium, sodium, uric acid.

o Sample to be taken before VES dosing.
p Complete blood count with differential and platelet count.
q Fasting (no food or drinks, except water, at least 8 hours prior to blood collection) glucose and lipid panel (total cholesterol, high-density lipoprotein, direct low-density lipoprotein, 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 to draw blood for the metabolic assessments.
r Creatinine clearance according to the Cockcroft-Gault formula: Female Estimated Creatinine Clearance = [(140–− age in years) × (weight in kg)]/[72 × (serum creatinine in mg/dL)] × 0.85.
s Serum follicle-stimulating hormone test is required for female participants < 54 years old who have stopped menstruating for ≥ 12 months, but are not permanently sterile or do not have documentation of ovarian hormonal failure.
t Hepatitis B virus blood panel will be performed at screening (hepatitis B virus surface antigen, hepatitis B virus surface antibody, and hepatitis B virus core antibody). Hepatitis C antibody will also be performed.
u PK samples for VES will be collected at predose (≤ 5 minutes prior to dosing), 1, 2, 4, 8, 12, 24 (Day 1), and 48 hours (Day 2) after the first dose.
v Serum VRC07-523LS and CAP256V2LS PK collection on Day 7, at 0 hours (predose), end of infusion, 1, 2, 4, and 8 hours after end of infusion, and then at Days 8, 9, 14, 21, 28, 56, 84, 112, 133, 161, 189, 217, 245, 273, 301, 329, 343, 371, and 413.
w Plasma dolutegravir PK collections will be obtained at: Days 56, 84, 112, 133, 161, 189, 217, 245, 273, 301, 329, and for participants in Period 4B PK collections at Days 343, 371, and 413.
x From Period 2, if a confirmed rebound of HIV-1 RNA viral load ≥ 50 copies/mL occurs, the test should be completed weekly.
y Only if not previously conducted.
z Only at Day 147 visit.
aa Blood samples anti-VRC07-523LS and anti-CAP256V2LS antibody profiling from serum will be collected at the following timepoints: prebaseline/Day −13, Days 28, 56, 84, 112, 133, 161, 189, 217, 245, 273, 301, 329, 343, 371, and 413.
bb Days 161, 189, 217, 245, 273, 301, and 329 only.
cc Days 343, 371 and 413 only.
dd Lymph node and GALT biopsy will be collected from participants who provide additional consent at prebaseline/Day −13, Week 21 (beginning of Period 3), end-of-Period 3 visit, and the end-of-study visit. The samples can be collected within a window of ± 5 days.
ee Only at Day 134 visit.
ff Obtain HIV staging at detection using standard markers (eg, HIV-1 RNA, p24 antigen, fourth generation combination antigen/antibody enzyme-linked immunosorbent assay, HIV-1 Western blot), duration of viremia during acute HIV infection and peak HIV RNA
gg For Dose 3 only, 6 mg [3x2 mg tablets] or 8 mg [4x2 mg tablets]) will be administered per discussion with and approval from the Gilead medical monitor based on safety and tolerability of prior doses.
hh For Doses 4 to 10, 6 mg [3x2 mg tablets] or 8 mg [4x2 mg tablets]) will be administered per discussion with and approval from the Gilead medical monitor based on safety and tolerability of prior doses.

Appendix 2. Data Collection of Disaster or Public Health Emergency Data

This appendix describes the clinical trial site collection of Disaster or Public Health Emergency data pertaining to missed/virtual visits and the data processing algorithm that will be used to determine which visits are missing and which visits are virtual.

1) Data Collection

A Disaster or Public Health Emergency supplement to the eCRF Completion Guidelines (CCG) was provided by Clinical Data Management to instruct clinical trial sites with data entry expectations pertaining to scenarios related to the Disaster or Public Health Emergency. If a visit was missed, sites were instructed to enter "Visit missed due to {specify}" and if an in-person visit was conducted virtually, sites were instructed to enter "Virtual visit due to {specify}".

2) Determination of Missed and Virtual Visits

Natural Language Processing (NLP) will be used to search the CRF comment fields to identify instances of "{specify}", "Virtual", or synonyms (see Table 12-1 for example for COVID-19 pandemic). The search terms will be maintained in a global lookup table and can be modified to tune the NLP model. Any comments with {specify} search terms, "Missed visit" or "Virtual visit will be assigned as follows:

i) If {specify}terms are identified through NLP and the visit date is missing, then result is "Missed Visit"

ii) If {specify}and Virtual terms are identified through NLP for a visit, then result is "Virtual Visit". When there are multiple records for the same participant and the same visit, if one record could be categorized as "Virtual Visit", all records associated with this participant and this visit will be categorized as "Virtual Visit"

iii) Otherwise result is missing

Table 12-1. Example Search Terms for "COVID-19" and "Virtual" Used to Identify Missed/Virtual Visits.

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

Appendix 3. Laboratory Values

Calcium Corrected for Albumin

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

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

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

Estimated Glomerular Filtration Rate

The following formulae will be used to calculate the estimated glomerular filtration rate using Cockcroft-Gault formula ($eGFR_{CG}$):

$eGFR_{CG}$ (mL/min) = [(140 – age (yrs)) × weight (kg) × (0.85 if female)] / (SCr (mg/dL) × 72),

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

Appendix 4. Adverse Events Category

An adverse event record will be flagged for an AE category for analysis in the raw Adverse Events dataset if its MedDRA PT is included in the pre-specified MST list for the corresponding AE category, under MedDRA Version 28.0.

AE Category MST Name (Variable Name)	Preferred Terms
Cytokine Release Syndrome - HIV Cure therapy	• Arthralgia • Capillary leak syndrome • Chills • Fatigue • Headache • Hypotension • Hypoxia • Influenza • Influenza like illness • Malaise • Myalgia • Nausea • Pyrexia • Shock • Tachypnoea • Vomiting • Cytokine storm • Systemic inflammatory response syndrome • Cytokine release syndrome • Haemophagocytic lymphohistiocytosis • Multiple organ dysfunction syndrome • Chronic inflammatory response syndrome • Primary stabbing headache • Immunotoxicity • Immune effector cell-associated HLH-like syndrome

GS-US-382-5445-Final Analysis-SAP-v1.0

ELECTRONIC SIGNATURES

Signed by	Meaning of Signature	Server Date (dd-MMM-yyyy hh:mm:ss)
PPD	Biostatistics eSigned	11-Jun-2025 18:45:37
PPD	Clinical Development eSigned	11-Jun-2025 19:37:28
PPD	Clinical Pharmacology eSigned	13-Jun-2025 18:42:34