Reporting and Analysis Plan

Study ID: 208090

Official Title of Study: Reporting and Analysis Plan for A Phase III, randomized, multicenter, open-label, non-inferiority study evaluating the efficacy, safety and tolerability of switching to dolutegravir/lamivudine fixed dose combination in HIV-1 infected adults who are virologically suppressed

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Title	:	Reporting and Analysis Plan for A Phase III, randomized, multicenter, open-label, non-inferiority study evaluating the efficacy, safety and tolerability of switching to dolutegravir/lamivudine fixed dose combination in HIV-1 infected adults who are virologically suppressed
Compound Number	:	GSK1349572+GR109714 (GSK3515864)
Effective Date	:	Refer to Document Date

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 208090.
- This RAP will be provided to the study team members to convey the content of the 208090 Statistical Analysis Complete (SAC) deliverables for the reporting effort up to Week 52.
- Separate RAPs will be developed at a later stage to convey the content of the End of Continuation Phase and CVW/PVW Sub-study deliverables.

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for Protocol 208090. The RAP is based on the following 208090 protocol versions Amendment 04 (05May2020), Amendment 04/CHI-1(20May2020)

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

The following changes were made to the agreed upon sections in the protocol [(Dated: 14 NOV 2018)].

Section # and Name	Description of Change and Rationale
Exploratory Objective/Endpoints: • Protocol Section 3.0	• Addition of an exploratory objective/endpoints that were not specified in the protocol Section 3.0. o Objective: o To evaluate the effect of subject characteristics (e.g., demographic factors, Baseline CD4) on antiviral and immunological responses to DTG/3TC compared to CAR o Endpoints: o Proportion of subjects by subgroups with plasma HIV-1 RNA <50 c/mL using the Snapshot algorithm at Weeks 24 and 48 o Change from Baseline in CD4+ cell counts at Weeks 24 and 48 by patient subgroups

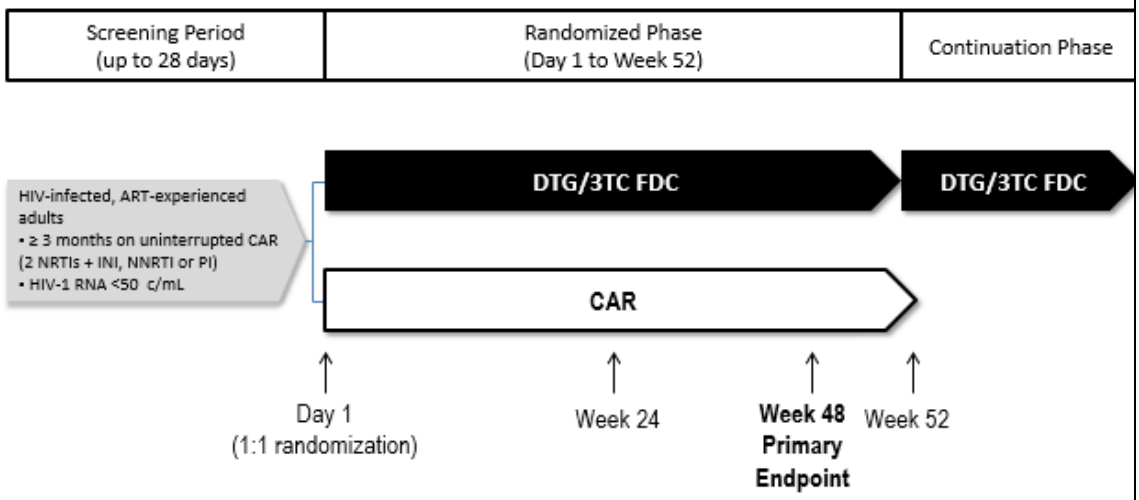
2.2. Study Objective(s) and Estimand(s) / Endpoint(s)

Objectives	Estimands / Endpoints
Primary	**Primary**
To demonstrate the non-inferior antiviral activity of switching to DTG/3TC FDC once daily compared to continuation of CAR over 48 weeks in virologically suppressed adults living with HIV-1	Proportion of subjects with plasma HIV-1 RNA ≥50 c/mL) endpoint as per FDA snapshot category at Week 48 using the Snapshot algorithm for the ITT-E population
Secondary	**Secondary**
To demonstrate the antiviral activity of switching to DTG/3TC FDC once daily compared to continuation of CAR over 48 weeks	Proportion of subjects with plasma HIV-1 RNA <50 c/mL at Week 48 using the Snapshot algorithm for the ITT-E population
To evaluate the antiviral activity of switching to DTG/3TC FDC once daily compared to continuation of CAR over 24 weeks	• Proportion of subjects with plasma HIV-1 RNA ≥50 c/mL) endpoint as per FDA snapshot category at Week 24 • Proportion of subjects with plasma HIV-1 RNA <50 c/mL at Week 24 using the Snapshot algorithm for the ITT-E population

Objectives	Estimands / Endpoints
To evaluate the immune effects of DTG/3TC FDC once daily compared to continuation of CAR	• Change from Baseline in CD4+ cell count and in CD4+/CD8+ cell counts ratio at Weeks 24 and 48 • Incidence of disease progression (HIV-associated conditions, AIDS, and death) through Weeks 24 and 48
To evaluate the safety and tolerability of DTG/3TC FDC once daily compared to CAR over time	• Incidence and severity of adverse events (AEs) and laboratory abnormalities • Proportion of subjects who discontinue treatment due to AEs
To evaluate the safety and tolerability of DTG/3TC FDC once daily in those with creatinine clearance of between 30-49 mL/min/1.73m^2 compared to those with a creatinine clearance of ≥50 mL/min/1.73m^2	• Incidence and severity of AEs and laboratory abnormalities • Proportion of subjects who discontinue treatment due to AEs
To evaluate the effects of DTG/3TC FDC once daily on fasting lipids over time compared to CAR	Change from Baseline in fasting lipids at Weeks 24 and 48
To assess viral resistance in participants meeting Confirmed Virologic Withdrawal (CVW) Criteria	Incidence of observed genotypic and phenotypic resistance to ARVs for participants meeting CVW Criteria
To assess health related quality of life for participants treated with DTG/3TC FDC compared to CAR	Change from Baseline in health status using HIV TSQ at Weeks 24 and 48 (or Withdrawal from the study) and SDM at Weeks 24, 48 and every 24 weeks during the continuation phase (or Withdrawal from the study)
Tertiary/Exploratory	**Tertiary/Exploratory**
To assess willingness to switch for participants treated with DTG/3TC FDC compared to CAR	Reasons for Willingness to Switch at Day 1
To evaluate renal (in urine and blood), bone (in blood), inflammatory (in blood) biomarkers and insulin resistance in participants treated with DTG/3TC FDC compared to CAR	Change from Baseline in renal, bone and inflammatory biomarkers and homeostasis model of assessment-insulin resistance (HOMA-IR) at Weeks 24 and 48
To evaluate biomarkers of telomerase[a] function in participants treated with DTG/3TC FDC compared to CAR.	Change from baseline in biomarkers of telomerase function at Week 48
[a] Separate RAP and report will be produced for biomarkers of telomerase	

2.3. Study Design

Overview of Study Design and Key Features



Design Features	• This is a 52-week, Phase III, randomized, open-label, active-controlled, multicenter, parallel-group non-inferiority study. The study will include a Screening Phase (up to 28 days), a Randomized Phase (Day 1 up to Week 52), and a Continuation Phase (post Week 52).
Dosing	• Patients receiving DTG/TC will receive DTG (50mg)/3TC (300mg) FDC once daily. Patients receiving CAR will receive the dose as determined by their prescribing physician.
Time & Events	• Refer to Appendix 2: Schedule of Activities
Treatment Assignment	• Approximately 490 subjects who are stable on CAR will be randomized 1:1 to switch to DTG/3TC FDC once daily (DTG/3TC arm) for up to 52 weeks, or to continue their CAR for 52 weeks (if HIV1 RNA <50 c/mL at Week 48 (or at Week 52 if re-tested))
Interim Analysis	• An analysis will be conducted to evaluate the primary objective of the protocol when all subjects have completed their Week 48 visit and any HIV-1 RNA re-tests as appropriate. An interim analysis will be conducted when all subjects have completed their Week 24 visit and any HIV-1 RNA re-tests as appropriate (see Blinding Agreement for more details). To minimise bias, the Week 24 results will not be shared with subjects and investigators, or presented externally until after the last subject completes their Week 48 visit
Sub-study	• A sub-study is planned in this study that will evaluate and determine the virologic response to subsequent regimens of subjects in DTG/3TC FDC arm with HIV-1 RNA ≥ 50 c/mL. The evaluation period will start from the time the subjects is discontinued from the 208090 study for confirmed virologic withdrawal (CVW) or precautionary virologic withdrawal (PVW) criteria while on DTG/3TC FDC and will last for up to 12 months. A sub-study RAP will be developed in a separate document.

See study protocol for further details

2.4. Statistical Hypotheses / Statistical Analyses

This study is designed to show that the antiviral effect of switching to a simplified two-drug regimen of DTG/3TC FDC once-daily is non-inferior to continuation on CAR.

Non-inferiority in the proportion of subjects with plasma HIV-1 RNA ≥ 50 c/mL at Week 48 as measured by using the FDA (Food and Drug Administration) Snapshot algorithm (see Appendix 11), can be concluded if the upper bound of a two-sided 95% confidence interval for the difference in the proportion of subjects with plasma HIV-1 RNA ≥ 50 c/mL between the two treatment arms (DTG/3TC - CAR) is less than 5%. If r_d is the response rate on DTG/3TC and r_c is the response rate on CAR, then the hypotheses can be written as follows:

$$H_0: r_d - r_c \geq 5\% \qquad H_1: r_d - r_c < 5\%$$

3. PLANNED ANALYSES

3.1. Interim Analyses

An interim analysis will be performed at Week 24. To minimise bias, the results of the Week 24 results will not be shared with subjects and investigators or presented externally until after the last subject completes their Week 48 visit. Please refer to the Blinding Agreement for more details.

The planned analysis at Week 24 will be performed after the completion of the following sequential steps:

- Last subject has completed their visit at Week 24 as defined in the protocol, including any re-test as appropriate.
- All required database cleaning activities have been completed and, final database release and database freeze have been declared by Data Management.
- All criteria for unblinding[1] the randomization codes at Week 24 have been met.

No adjustment for multiplicity will be made as the Week 24 analyses will be secondary, however non-inferiority at Week 24 will be declared if the upper bound of a two-sided 95% confidence interval for the difference in HIV-1 RNA $\geq$ 50 c/mL rates between the two treatment arms is less than 5%[2].

An IDMC is instituted to ensure external objective medical and/or statistical review of efficacy and safety to protect the ethical interests and well-being of subjects and to protect the scientific validity of the study. An ad-hoc review of data by the IDMC will be triggered whenever the number of confirmed virologic withdrawals (CVWs) exceeds thresholds pre-specified in the IDMC charter. Full details of the methods, timing, decision criteria and operating characteristics are pre-specified in the IDMC Charter. Details of the analyses and outputs provided to the IDMC are detailed in an IDMC RAP.

1. Note that analyses for time points will be performed when subjects complete visits relevant to that time point i.e. Week 24 analysis takes place when the last patient has completed their Week 24 visit..
2. Please refer to Section 7.1.5.1 for details and conditions for presentation of test for superiority

3.2. Final Analyses

The primary analysis is at Week 48. An additional analysis will be performed at the end of the continuation phase .

The planned analyses at Weeks 48 and end of continuation phase[3] will be performed after the completion of the following sequential steps:

- Last subject has completed their relevant visit at week 48 (or end of continuation) as defined in the protocol, including any re-test as appropriate.
- All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.
- All criteria for unblinding the randomization codes at Week 48 have been met.

Further data cuts and analyses may be conducted as necessary in support of regulatory submissions and publications.

The End of Continuation Phase and sub-study analyses will be covered by separate RAPs.

3. Note that analyses for time points will be performed when subjects complete visits relevant to that time point i.e. Week 48 analysis takes place when the last patient has completed their Week 48 visit, and not when they have completed their Week 48 and end of continuation phase.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• Comprises Screened for inclusion in the study, including screen-failures. • This population will be based on the treatment to which the subject was randomized. Screen-failures will be categorised as "Non-randomized".	• Study Population
Randomized	• The Randomized population will consist of all subjects who are randomized in the study • Any subject who receives a treatment randomization number will be considered to have been randomized.	• Study Population
Intent-to-Treat (ITT)	• Comprises all randomized subjects • Subjects will be assessed according to the treatment to which the subject was randomized regardless of treatment they actually received. • Any subject receiving a treatment randomization number will be considered to be randomized.	• Efficacy (sensitivity analyses)
Intent-To-Treat Exposed (ITT-E)	• Comprises all randomized subjects who receive at least one dose of study treatment either DTG/3TC or CAR. • This population will be based on the treatment to which the subject was randomized.	• Study Population, Efficacy and Health Outcomes
Per-Protocol (PP)	• This population will consist of subjects in the ITT-E Population with the exception of significant protocol violators. • Protocol deviations that would exclude subjects from the PP population are defined in Section 4.1 (Protocol Deviations) and Appendix 1 (Protocol Deviation Management and Definition for Per-Protocol Population).	• Efficacy (Sensitivity Analysis)
CVW	• Comprises all subjects in the ITT-E population who have met the derived CVW criteria (see Section 15.6.3)	• Genotypic • Phenotypic • Efficacy

Population	Definition / Criteria	Analyses Evaluated
potential Precautionary Virologic Withdrawal (pPVW)	• Comprises subjects in the ITT-E population having 2 consecutive measurements between 50 and 200 c/mL. The current HIV-1 RNA values must be below 200 c/mL, but the previous HIV-1 RNA can also have been >=200 c/mL	• Genotypic • Phenotypic
Safety	• Comprises all subjects who receive at least one dose of study treatment either DTG/3TC or CAR. • This population will be based on the treatment the subject actually received[4].	• Safety

NOTES:

- Please refer to Appendix 16: List of Data Displays which details the population to be used for each display being generated.

4. As recorded on IVRS. If the randomized treatment is incorrect, the actual treatment will only be recorded in IVRS through sponsor intervention

4.1. Protocol Deviations

Term	Definition
Study Deviation Rules Document	The document describing study deviations (and associated coding/naming conventions) that may be identified during a study and the frequency of study deviation reviews.
Protocol Deviation (PD)	Any departure from study-specific requirements specified in a protocol. Subsets of protocol deviations are categorized as important or significant.
Important Protocol Deviations	A subset of protocol deviations that may significantly impact the completeness, accuracy, and/or reliability of the study data or that may significantly affect a subject's rights, safety, or well-being. All important deviations have a Violation Flag in CTMS and are associated with a Rule Number.
Significant Protocol Deviations	Considered a subset of important protocol deviations, typically impacting efficacy assessments, which lead to the exclusion from the per-protocol population. All significant deviations are captured in CTMS and are associated with a Rule Number.

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management , patient assessment) will be summarised and listed.

Separately, important deviations which result in exclusion from analysis populations and events that results in exclusion from the analysis population will be summarised and listed (see Appendix 1).

The COVID-19 Pandemic has the potential to impact subject visit completion. This may result in PDs being reported which are related to COVID-19 rather than study non-compliance by subjects or sites. As a result, all COVID-19 specific PDs identified using "COVID-19" prefix as defined in the protocol deviations specification document will be summarised and listed.

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Deviation Rule Document.

- Data will be reviewed prior to unblinding and freezing of the database with the aim of capturing and categorising all important deviations.
- This dataset will be the basis for the summaries and listings of protocol deviations.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Description	Order [1]
DTG/3TC	1
CAR	2

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.

Treatment comparisons will be displayed as follows using the descriptors as specified:

1. DTG/3TC vs CAR

5.2. Baseline Definitions

For all endpoints (unless otherwise stated) the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline.

Unless otherwise stated, if baseline data are missing no derivation will be performed and baseline will be set to missing.

Unless otherwise specified, the baseline definitions specified in the table below will be used for derivations for endpoints/parameters and indicated on summaries and listings.

Definition	Reporting Details
Change from Baseline	= Post-Dose Visit Value – Baseline
% Change from Baseline	= 100 x [(Post-Dose Visit Value – Baseline) / Baseline]

5.3. Multicentre Studies

Data will be summarised for all centres combined. Country will be included as an exploratory subgroup for analyses of specific endpoints.

5.4. Examination of Covariates, Other Strata and Subgroups

5.4.1. Covariates and Other Strata

- Table 1 presents the covariates that may be used in descriptive summaries and statistical analyses, some of which may also be used for subgroup analyses.
- Additional covariates of clinical interest may also be considered.

Table 1 List of Covariates for Descriptive Summaries and Statistical Analyses

Details	Endpoints					
	Renal Biomarkers	**Bone Biomarkers**	**Inflammatory Biomarkers**	**HOMA-IR , HbA1c**	**Weight, BMI/Lipids**	**HO (SDM and HIVTSQ)**
Randomization is stratified by baseline third agent class: • Baseline third agent class (PI, INI, NNRTI). for analysis purposes, randomization strata will be derived using eCRF data, even if this differs from the strata captured in IVRS (details of how this is derived can be found in Section 15.6.8) All statistical analyses will adjust for the above randomization strata, unless stated otherwise. Treatment-by-Strata interactions will be assessed as specified in the analysis sections.	Y	Y	Y	Y	Y	Y
Age (years): (Continuous)	Y	Y	Y	Y	Y	Y
Gender: Male & Female	Y	Y	Y	Y	Y	Y
Baseline CD4+ cell count (continuous)	Y	Y	Y	Y	Y	
Race (White, Black or African American, Asian, Other)	Y	Y	Y	Y	Y	Y
BMI (continuous)	Y	Y	Y	Y		
Smoking status (Never vs. Former vs. Current Smoker)		Y	Y			
Diabetes mellitus (Yes vs. No)	Y			Y (for HbA1c)		
Hypertension (Yes vs. No)	Y			Y		
HCV-coinfection (Yes vs. No)			Y			
Baseline value of the endpoint*	Y	Y	Y	Y	Y	Y

* Baseline value will be continuous, and if the outcome is log-transformed the baseline value will be log-transformed as well

5.4.2. Examination of Subgroups

The list of subgroups may be used in descriptive summaries and statistical analyses. Additional subgroups of clinical interest may also be considered.

- If the percentage of subjects is small within a subgroup, then the subgroup categories may be refined prior to unblinding the trial.

If the category cannot be refined further, then descriptive rather than statistical comparisons may be performed for the particular subgroup.

Subgroup	Subgroups
Randomization Strata	Randomization is stratified by baseline third agent class: • Baseline third agent class (PI, INI, NNRTI). For analysis purposes, randomization strata will be derived using eCRF data, even if this differs from the strata captured in IVRS All statistical analyses will adjust for the above randomization strata, unless stated otherwise. Treatment-by-Strata interactions will be assessed as specified in the analysis sections.
Demographic and Baseline Characteristics	• Age (years): o <35, 35 - 49, ≥50, and <50 vs. ≥50 o <60 and ≥60 may also be performed if specifically required for regulatory purposes • Gender: Male & Female • Race: o White, Black or African American, Asian, Other o White, Non-White • Country • Baseline CD4+ cell count: o <500, ≥500 cells/mm^3 • CDC HIV-1 classification o HIV infection stage 0 o HIV infection stage 1 o HIV infection stage 2 o HIV infection stage 3 (AIDS) o HIV infection stage unknown • Baseline Creatinine Clearance o 30-49 mL/min/1.73m^2 o ≥50 mL/min/1.73m^2

Subgroup	Subgroups
	• Baseline concerns with long-term side effects of their current ART (PCLTT): (Yes/No) *

* Subgroup is for Health outcome analysis. This is derived from Willingness to switch questionnaire with baseline response given as "Concerned about long-term side effects" as the reason for willingness to participate in a clinical study where their current HIV medication may be switched.

Subgroup analyses for endpoints will be presented as shown in the Table 2.

Table 2 List of Subgroup Variables for Descriptive Summaries and Statistical Analyses

	Endpoint					
Subgroup	**Proportion of patients with plasma HIV-1 RNA <50[1] c/mL[2]**	**Summary of Study Snapshot outcomes (Plasma HIV-1 RNA ≥/< 50 c/mL)**	**CD4+ Cell Count and CD4+/CD8+ Ratio Change from Baseline**	**AEs[3]**	**Clinical Chemistry, Hematology and Liver Chemistries**	**HO (SDM and HIVTSQ)**
Baseline third agent class (PI, INI, NNRTI,)	Y	Y	Y	Y		Y
Age (years): <35, 35 - 49, ≥50	Y	Y	Y	Y		
Age (years): <50, ≥50	Y	Y				
Gender: Male & Female	Y	Y	Y	Y		
Country	Y	Y				
Race: White, Black or African American, Asian, Other	Y	Y	Y	Y		
Race: White, non-white	Y	Y	Y			
Baseline CD4+ cell count: <500, ≥500 cells/mm3	Y	Y	Y	Y		
CDC HIV-1 classification:: HIV infection stage 0, 1, 2, 3 (AIDS), Unknown	Y	Y	Y	Y		
Baseline Creatinine Clearance: 30-49 mL/min/1.73m^2, ≥50 mL/min/1.73m^2				Y	Y	
Baseline concerns about long-term side effects of their current HIV regimen (PCLTT): (Yes/No)						Y

1. A sensitivity analysis will also be performed for the following endpoint: HIV-1 RNA <40 c/mL and Target Not Detected Status. See Section 7.2.5 for more details.
2. Includes forest plot for unadjusted difference of patients with plasma HIV 1 RNA <50 c/mL between treatment arms.

3. Subgroup analyses will be presented for the following analyses: Adverse Events by System Organ Class (see Appendix 16 Full Data Displays for more information)

5.5. Multiple Comparisons and Multiplicity

The primary comparison of interest is the comparison between DTG/3TC and CAR for the primary endpoint in the ITT-E population. This analysis will be adjusted for by the actual stratification factor as determined from the eCRF data (not as recorded in IVRS) randomisation.

No adjustment for multiplicity is required as there is only one primary comparison of interest.

5.6. Other Considerations for Data Analyses and Data Handling Conventions

Other considerations for data analyses and data handling conventions are outlined in the appendices:

Section	Component
Section 15.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
Section 15.2	Appendix 2: Schedule of Activities
Section 15.3	Appendix 3: Assessment Windows
Section 15.4	Appendix 4: Study Phases and Emergent Adverse Events
Section 15.5	Appendix 5: Data Display Standards & Handling Conventions
Section 15.6	Appendix 6: Derived and Transformed Data
Section 15.7	Appendix 7: Reporting Standards for Missing Data
Section 15.8	Appendix 8: Values of Potential Clinical Importance
Section 15.9	Appendix 9: Population Pharmacokinetic (PopPK) Analyses
Section 15.10	Appendix 10: Time to Event Details
Section 15.11	Appendix 11: Snapshot
Section 15.12	Appendix 12: Modified Snapshot Algorithm Details
Section 15.13	Appendix 13: Abbreviations & Trade Marks
Section 15.14	Appendix 14: Model Checking and Diagnostics for Statistical Analyses
Section 15.15	Appendix 15: Test of Homogeneity: Fleiss, Liu & Kelly Method
Section 15.16	Appendix 16: List of Data Displays
Section 15.17	Appendix 17: Example Mock Shells for Data Displays

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the Intent-To-Treat Exposed (ITT-E) population, unless otherwise specified.

Table 3 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 16: List of Data Displays.

Table 3 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated	
	Table	Listing
Randomization		
Randomization		Y [1]
Misrandomized Strata or Treatment	Y	
Subject Disposition		
Subjects Enrolled by Country and Site ID [2]	Y	Y
Subjects Enrolled by Country and Site ID relative to COVID-19 Pandemic measures	Y	
Country Level Listing of Start Dates of COVID-19 Pandemic Measures		Y
History of Rescreened Subjects [2]		Y
Reasons for Screen Failure [2]	Y	Y
Subject Disposition	Y [3,4]	
Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic	Y	
Treatment Status and Reasons for Discontinuation of Study Treatment by relationship to COVID-19 Pandemic	Y	
Reasons for Withdrawal by Visit	Y	Y
Study Visit Dates		Y
Visits Impacted by COVID-19 Pandemic[11]	Y	Y
Populations Analysed		
Study Populations [2]	Y	Y
Protocol deviations		
Important Protocol Deviations by Relationship to COVID-19	Y	Y
Deviations leading to exclusion from PP	Y	Y

Inclusion and Exclusion Criteria Deviations		Y
Non-Important Protocol Deviation Related to COVID-19		Y
Demography and baseline characteristics		
Demographic Characteristics [5]	Y	Y
Summary of Age Ranges	Y	
Race & Racial Combinations [6]	Y	Y
Hepatitis C Status	Y	Y
CDC Classification of HIV infection at Baseline	Y	Y
HIV Risk Factor	Y	Y
Cardiovascular Risk Assessments at Baseline	Y	Y
Distribution of CD4+ Cell Counts	Y	
Distribution of HIV-1 RNA (c/mL)	Y	
Distribution of CD4+/CD8+ cell count ratio	Y	Y
Medical Conditions, Concomitant Medications & Antiretroviral Therapy		
Medical Conditions (Current and Past)	Y	Y
Medical Conditions: Sub-conditions (Current/Past)	Y	
Concomitant Medications (non-ART)	Y [7]	Y [8]
Prior and Concomitant ART Medications	Y	Y [9]
Baseline third agent class (Strata) [10]	Y	Y
Lipid Modifying agents (Baseline and Post-Baseline)	Y	
Other		
History of Depression and Anxiety at Baseline	Y	

NOTES:

- Y = Display Generated, T = Tables, L = Listings, IP = Investigational Product

1. ITT-E. One listing of subjects randomized but not treated, and one listing of planned and actual treatment strata.
2. Screened population.
3. Subject Accountability by Phase (Overall, Randomized Phase, Continuation Phase)
4. Subjects who have not been recorded as withdrawing from the study in the respective phase will be categorized as “Ongoing at time of the analysis” for summary purposes.
5. Age, sex, ethnicity, weight, height, BMI (kg/m^2) and child-bearing potential collected at screening.
6. The five high level FDA race categories and designated Asian subcategories will be summarised along with all combinations of high level categories which exist in the data. The nine race categories collected will be summarised along with categories for mixed race. A by-subject listing of race will also be produced.
7. Summarised by Ingredient ATC Level 1
8. One listing for concomitant non-ART medications and one listing showing the relationship between verbatim text, ingredient and ATC Level 1.
9. One listing for Prior ART, one listing for concomitant ART and one listing showing the relationship between verbatim text, ingredient, combination and ATC Level 4.
10. Based on the actual third agent class that subjects were classified into according to data captured on the eCRF.
11. Visits impacted by COVID-19 Pandemic will also be presented by stacked bar chart

7. EFFICACY ANALYSES

7.1. Primary Efficacy Analyses

The primary treatment effect to be estimated will be the effect on the composite virologic outcome at Week 48, using the FDA (Food and Drug Administration) Snapshot algorithm. The variable is the binary response indicating the virologic outcome category of plasma HIV-1 RNA ≥50 copies/mL (c/mL) at Week 48 and the summary measure is the difference in the percent of subjects with plasma HIV-1 RNA ≥50 c/mL at Week 48 between each treatment group. The population is all subjects in the Intent-to-Treat Exposed (ITT-E) population. The individual components of the estimand are detailed as follows.

7.1.1. Endpoint / Variables

The primary endpoint is the percent of subjects with plasma HIV-1 RNA ≥50 c/mL at Week 48 using the FDA Snapshot algorithm (see Section 15.11).

The primary endpoint is the binary response indicating the virologic outcome category of plasma HIV-1 RNA ≥50 c/mL at Week 48 using the FDA Snapshot algorithm (See Appendix 11). The other Snapshot outcomes (HIV-1 RNA <50 c/mL and no virologic data at Week 48 Window) will be collapsed into the non-response category.

7.1.2. Summary Measure

Difference in the percent of subjects with plasma HIV-1 RNA ≥50 c/mL at Week 48, defined by the FDA snapshot algorithm (see Appendix 11), between each treatment groups (DTG/3TC – CAR).

7.1.3. Population of Interest

The primary efficacy analyses will be based on the Intent-To-Treat Exposed (ITT-E) population (defined in Section 4) unless otherwise specified.

7.1.4. Strategy for Intercurrent (Post-Randomization) Events

A treatment policy strategy will be used for intercurrent events such as discontinuations, missing plasma HIV-1 RNA samples and change in background regimen are handled using the Snapshot algorithm (see Section 15.11), which details how to assign each subject's virologic outcome.

7.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 16: List of Data Displays and will be based on GSK data standards and statistical principles commonly applied in GSK HIV-1 trials.
Table 4 provides an overview of the planned efficacy analyses, with full details of data displays being presented in Appendix 16: List of Data Displays.

Table 4 Overview of Planned Primary Efficacy Analyses

Endpoint	Absolute						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Percent of Subjects with plasma HIV 1 RNA ≥50 c/mL at week 48 – Snapshot							
Primary Analysis	Y [1]		Y				
Sparse Data Analysis	Y [2]						

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

[1] Generated using the 'Intent-to-Treat Exposed' (primary), 'Per-Protocol' and 'Intent-to-Treat' (sensitivity) populations.
[2] See methodology section for more information.

7.1.5.1. Statistical Methodology Specification

Endpoint
The binary response indicating the virologic outcome category of plasma HIV 1 RNA ≥50 c/mL at Week 48 using the FDA Snapshot algorithm (see Appendix 11).
Model Specification
The primary efficacy endpoint will be analysed using a stratified analysis for proportions with Cochran-Mantel-Haenszel (CMH) weights, adjusting for baseline third agent class (PI, INI, NNRTI). The CMH estimate of the adjusted treatment difference will be calculated as a weighted average of strata-specific estimates of the treatment difference calculated within each of the following three Baseline analysis strata: ○ Baseline third agent: PI ○ Baseline third agent: INI ○ Baseline third agent: NNRTI If n_k is the number of DTG/3TC treated subjects, m_k is the number of PI-, INI-, or NNRTI-based ART treated subjects, and $N_k = n_k + m_k$ is the total number of subjects in the *k*th stratum, then the CMH estimate is given by:

$$\hat{d}_{cmh} = \frac{\sum W_k \hat{d}_k}{\sum W_k}$$

where,

$$W_k = \frac{n_k m_k}{N_k}$$

are CMH weights and d_k are estimates of the differences in proportions of subjects with plasma HIV-1 RNA ≥50 c/mL between the two treatment arms, $r_{DTG/3TC}$ -r_{CAR}, for the *k*th strata.

The corresponding two-sided 95% CI will be calculated as

$$\hat{d}_{cmh} \pm 1.96 \times \sqrt{\hat{\text{var}}(\hat{d}_{cmh})}$$

Where the variance estimator (Sato ,1989) is consistent in both sparse data and large strata and is given below.

$$\hat{\text{var}}\left(\hat{d}_{cmh}\right) = \frac{\hat{d}_{cmh}\left(\sum P_k\right) + \sum Q_k}{\left(\sum n_k m_k / N_k\right)^2} = \frac{\hat{d}_{cmh}\left(\sum P_k\right) + \sum Q_k}{\left(\sum W_k\right)^2},$$

where

$$P_k = \frac{n_k^2 y_k - m_k^2 x_k + n_k m_k (m_k - n_k)/2}{N_k^2}$$

$$Q_k = \frac{x_k (m_k - y_k)/N_k + y_k (n_k - x_k)/N_k}{2}.$$

With x_k and y_k corresponding to the number of subjects with HIV-1 RNA ≥50 c/mL at Week 48 as determined by the FDA Snapshot algorithm (See Appendix 11) for treatment and comparator, respectively, for the k^{th} stratum.

Model Checking & Diagnostics

Not applicable

Model Results Presentation

Adjusted CMH estimate of the difference in the proportion of subjects with plasma HIV-1 RNA ≥ 50 c/mL between each treatment group (DTG/3TC – CAR) and corresponding 95% confidence interval will be presented.

Non-inferiority will be concluded if the upper bound of the two-sided 95% confidence interval (CI) for the CMH adjusted difference in the proportion of patients with plasma HIV-1 RNA ≥ 50 c/mL

between each treatment group (DTG/3TC – CAR) is less than 5%. The p-value for non-inferiority based on a non-inferiority margin of 5% will also be presented. 95% confidence intervals for the percent of subjects with virologic failure by treatment group.

If the analysis shows non-inferiority, then a superiority hypothesis will be tested at the two-sided 5% level of significance. Superiority favoring DTG/3TC will be declared if the upper bound of two-sided confidence interval is below 0%. If superiority is declared, the p-value for superiority will also be presented.

Subgroup Analyses

- Subgroup analyses will not be performed for this endpoint

Sensitivity and Supportive Analyses

1. Per-Protocol population analysis:
   - To assess the impact of significant protocol deviations, statistical analysis will be repeated using the Per-protocol population and compared for consistency with the results from the primary ITT-E population analysis. If both analyses show non-inferiority then the hypothesis that the antiviral effect of treatment with DTG/3TC is superior to treatment with CAR will be tested at the two-sided 5% level of significance.
2. Intent-to-Treat population analysis:
   - Statistical analysis will be repeated using the Intent-to-Treat population and compared for consistency with the results from the ITT-E and PP populations.
   - In this analysis, subjects randomized but not exposed to study treatment will be classified as “having no virologic data”.
3. Separate supportive analyses will be performed to enable the assessment of the homogeneity of the treatment difference across strata.
   The weighted least squares chi-squared statistic of [D’Agostino, 2008,Fleiss, 1981] will be used to test for one-way homogeneity of the treatment difference across the levels of each strata for baseline third agent class (PI, INI, NNRTI), with each categorical variable considered separately. Following Lui and Kelly [Lui, 2000], ½ will be added to each cell in any strata for which the stratum-specific rate estimates of either $r_{DTG/3TC}$ or r_{CAR} are zero or one, and tests will be one-sided. Tests of homogeneity will be assessed at the one-sided 10% level of significance. For details see Appendix 15.

   For each stratum in addition to the proportion of subjects with plasm HIV-1 RNA≥50 c/mL by treatment group and subgroup (with 95% CI type CI) as described in Appendix 15 , the p-value from the test of homogeneity will also be reported for each categorical stratification variable.
   These results will be used to assess the statistical assumption underlying the CMH stratified analysis procedure - namely the assumption on a common difference in unadjusted proportions across strata.
4. As the expected rate of HIV-1 RNA≥50 c/mL at week 48 is close to 0 (as a result of suppressed entry criteria), the 95% adjusted CI may be sensitive to the statistical method

used in its construction. Therefore, a sensitivity analysis using the Summary Score method (computed from the Miettinen-Nurminen CI limits of the stratum risk difference) will be performed to calculate the 95% CI of the adjusted treatment difference. This will be compared to the primary analysis method of CMH detailed above.

7.2. Secondary Efficacy Analyses

7.2.1. Endpoint / Variables

The secondary endpoints will include the following:

- The binary responses indicating the virologic outcome category of plasma HIV 1 RNA ≥50 c/mL at week 24 using the FDA Snapshot algorithm (see Appendix 11).
- The binary responses indicating the virologic outcome category of plasma HIV 1 RNA <50 c/mL at week 24 and Week 48 using the FDA Snapshot algorithm (see Appendix 11).
- CD4+ cell count at weeks 24 and 48.
- CD4+/CD8+ cell count ratio at weeks 24 and 48.
- Incidence of disease progression (HIV-associated conditions, AIDS, and death) through weeks 24 and 48

7.2.2. Summary Measure

- The number and percent of subjects with plasma HIV 1 RNA ≥50 c/mL at weeks 24 using the FDA snapshot algorithm (see Appendix 11).
- The number and percent of subjects with plasma HIV 1 RNA <50 c/mL at weeks 24 and 48 using the FDA snapshot algorithm (see Appendix 11).
- Change from baseline in CD4+ cell count at weeks 24 and 48.
- Change from baseline in CD4+/CD8+ cell count ratio at weeks 24 and 48.
- Incidence of disease progression (HIV-associated conditions, AIDS, and death) through weeks 24 and 48.

7.2.3. Population of Interest

The secondary efficacy analyses will be based on the ITT-E population.

7.2.4. Strategy for Intercurrent (Post-Randomization) Events

Intercurrent events such as discontinuations, missing plasma HIV-1 RNA samples and change in background regimen are handled using the FDA snapshot algorithm (see Appendix 11) which details how to assign each subject's virologic outcome. Intercurrent events will not be controlled for in disease progression and CD4+ cell count analyses.

7.2.5. Statistical Analyses / Methods

Table 5 provides an overview of the planned secondary efficacy analyses, with full details of data displays being presented in Appendix 16: List of Data Displays.

Table 5 Overview of Planned Secondary Efficacy Analyses

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Percent of Subjects with Plasma HIV-1 RNA ≥/ <50 c/mL– Snapshot														
Plasma HIV-1 RNA ≥50 c/mL analysis at Week 24	Y													
Plasma HIV-1 RNA <50 c/mL analysis at Week X [6]	Y[11]			Y[10]										
Study Outcomes (Plasma HIV-1 RNA ≥/ < 50 c/mL) based on the Snapshot at Week X [6]				Y			Y							
Plasma HIV-1 RNA <50 c/mL analysis By Visit through Week X [6]				Y										
Plasma HIV-1 RNA ≥50 c/mL analysis By Visit through Week X [6]				Y										
Plasma HIV-1 RNA <50 c/mL analysis by subgroup at Week X [6]				Y	Y [1]									
Study Outcomes (Plasma HIV-1 RNA ≥/ < 50 c/mL) based on the Snapshot by subgroup at Week X [6]				Y										

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Percent of Subjects with Plasma HIV-1 RNA ≥/ <50 c/mL– Modified Snapshot														
Study Outcomes (Plasma HIV-1 RNA ≥/ < 50 c/mL) at Week x [6]				Y			Y							
Confirmed Virologic Withdrawal (CVW)														
HIV-1 RNA distribution at time of suspected and confirmed Virologic withdrawal				Y			Y							
Potential Precautionary Virologic Withdrawal (pPVW)														
pPVW by Visit							Y							
Plasma HIV-1 RNA over time – Observed														
By Visit through Week X[6]							Y [2,9]				Y [5]			
CD4+ Cell Counts [3]														
By Visit through Week X [6]						Y [2]	Y				Y			Y
By Subgroup at Week X[6]											Y			
CD4+/CD8+ Cell Count Ratio [3]														
By Visit through Week X [6]						Y [2]	Y				Y			Y
By Subgroup at Week X[6]											Y			
Post-baseline HIV-1 Disease Progression [4]														
HIV Conditions including Recurrences at Week X [6,7]				Y			Y							
HIV Conditions excluding Recurrences at Week X [6,7]				Y										
HIV Disease Progressions at Week X [6,8]				Y										

NOTES :

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- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.

- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

1. Plot of 95% confidence intervals for unadjusted treatment difference in the proportion of subjects below 50 c/mL with overall and by subgroup.
2. Individual plasma HIV-1 RNA and CD4+ profiles only for subjects with at least one HIV-1 RNA levels ≥ 50 c/mL observed including at Day 1 and through withdrawal visit.
3. Using observed case (OC) data which contains the data that is available at a particular time point, with no imputation for missing values.
4. HIV disease progressions categories: CDC Category Stage 1 at enrolment to Stage 3 event; CDC Category Stage 2 at enrolment to Stage 3 event; CDC Category Stage 3 at enrolment to New Stage 3 Event; CDC Category Stage 0, 1, 2 or 3 at enrolment to Death.
5. Descriptive summary of the log10 change from baseline HIV-1 RNA by visit presented.
6. Week X refers to Week 24 and Week 48.
7. Stage 3 only.
8. Progression to Stage 3 or death.
9. Includes target detected/not detected flag see Section 15.6.3 for more information.
10. Repeated on the following endpoint: <40 c/mL and Target Not Detected Status.
11. Repeated on the following endpoints: 1) <40 c/mL only, 2) <40 c/mL and Target Not Detected Status.

7.2.5.1. Statistical Methodology Specification

Endpoint
• The binary responses indicating the virologic outcome category of plasma HIV 1 RNA ≥50 c/mL at week 24 using the FDA Snapshot algorithm (see Appendix 11). • The binary responses indicating the virologic outcome category of plasma HIV 1 RNA <50 c/mL at week 24 and Week 48 using the FDA Snapshot algorithm (see Appendix 11). • The analysis approach will follow the methods as described for the primary endpoint.
Model Specification
• Specification will be same as described for the primary endpoint
Model Checking & Diagnostics
• Same as described for the primary endpoint
Model Results Presentation
• Model presentation will be the same as described for the primary endpoint. • Percent of subjects with plasma HIV 1 RNA ≥50 c/mL will be analysed at Weeks 24. Percent subjects with plasma HIV 1 RNA <50 c/mL will be analysed at Week 24 and Week 48. • For Percent of subjects with plasma HIV-1 RNA <50 c/mL endpoint, non-inferiority of switching to DTG/3TC compared to continuation of CAR (as per FDA snapshot algorithm) will be assessed using a -12% non-inferiority margin. Non-inferiority will be concluded if the lower bound of a 2-sided 95% confidence interval for the difference in success rates between the two treatment arms is greater than -12%.
Subgroup Analyses
• Subgroup analyses will be performed for the percent of patients with plasma HIV 1 RNA <50 c/mL, study outcomes and unadjusted difference in proportion of patients with plasma HIV 1 RNA <50 c/mL between treatment arms at Week 24 and Week 48 endpoints (see Section 5.4.2).
Supportive Analyses

1. Supportive analysis based on the <50 HIV-1 RNA endpoint will be performed based on the same analysis for the following endpoints:
  • Percent of Subjects with Plasma HIV-1 RNA <40 c/mL at Week 24 and Week 48
  • Percent of Subjects with Plasma HIV-1 RNA <40 c/mL and Target Not Detected Status at Week 24 and Week 48
  • Percent of Subjects with Plasma HIV-1 RNA <40 c/mL and Target Not Detected Status at Week 24 and Week 48 by Baseline Third Agent Class
2. Proportion of subjects without virologic (ERDF) or virologic/tolerability (TRDF) failure:
  • Estimated using the Kaplan-Meier nonparametric method based on the time to Confirmed Virologic Withdrawal (CVW) criteria met or treatment-related (i.e. drug-

related AE, protocol defined safety stopping criteria, or lack of efficacy)/efficacy related discontinuation (i.e. lack of efficacy).

- The detailed algorithm for TRDF (and ERDF) is listed in Appendix 10. The estimate of the standard error used to derive confidence intervals for the difference in proportions between treatment groups will be based on Greenwood's formula [Kalbfleisch,1980]
- The estimated proportion of subjects without Confirmed Virologic Withdrawal and not discontinued due to treatment-related/efficacy-related reasons at Week 24 and at Week 48 will be presented by treatment group, along with estimated difference in proportions between treatment groups and its associated two-sided 95% CI.

3. Modified snapshot algorithm for study outcomes at Week 24 and Week48:

- Snapshot study outcomes will be repeated using the modified snapshot algorithm. The modified snapshot includes additional sub-reasons under "HIV-1 RNA≥50 c/mL" and "No Virologic Data" snapshot categories that are further divided by relationship to COVID-19. For details see Section 15.12 .

7.3. Exploratory Efficacy Analyses

- Subjects with plasma HIV-1 RNA <50 c/mL using the Snapshot algorithm at Week 24 and 48 by subgroup, based on the ITT-E population.
- Change from baseline CD4+ and CD4+/CD8+ ratio cell counts at Week 24 and 48 by subgroup.

These analyses have been specified in previous sections.

8. SAFETY ANALYSES

The safety analyses will be based on the Safety population, unless otherwise specified.

8.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 16: List of Data Displays.

Emergent AEs will be tabulated by treatment group and a total column. For AEs captured more than once, the most severe intensity will be included in summaries, and all events will be included in listings. For the purposes of summarising AE data, unless stated otherwise, the summaries will include post-baseline data.

For Week 24 and 48 analyses, outputs will be presented for the Randomized Phase unless otherwise specified. Safety data presented through weeks 24 and 48, will comprise all available safety data collected at that time point. For example, if some earlier recruiting subjects have reached Week 36 and have available safety data, this will be presented for the Week 24 analysis.

Table 6 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 15: List of Data Displays.

Table 6 Overview of Planned Safety Analyses

Endpoint	Absolute			
	Summary		Individual	
	T	F	F	L
Exposure				
Extent of Exposure	Y			Y [1]
Adverse Events [2]				
All AEs by SOC and PT[2, 7]	Y			Y
All AEs by Maximum Grade [2]	Y			Y [3]
Common AEs by Frequency [4]	Y	Y [5]		
Common Grade 2-5 AEs [4] by Frequency	Y			
Drug-Related AEs by SOC and PT	Y			Y
All Drug-Related AEs by SOC and Maximum Grade [2]	Y			
Common non-Serious AEs by SOC and PT (subjects and number of occurrences)	Y			
Common Drug-related Grade 2-5 AEs [4]	Y			
Drug-Related AEs leading to withdrawal from study	Y			
AEs Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment[8]	Y			Y
Serious and Other Significant AEs				
All SAEs by SOC	Y			
All Drug-Related SAEs by SOC	Y			
Serious AEs by SOC and PT	Y			
Reason for Considering as a Serious Adverse Event				Y
Possible Suicidality-Related Adverse Event (PSRAE)				Y [6]
Cardiovascular events				Y
Incidence of COVID-19 as reported as an AE and SAE[9]	Y			Y
Incidence of treatment discontinuation due to AE of COVID-19 infection[9]	Y			Y
Impact of Covid-19 on Assessment of Safety Based on COVID-19 eCRF				
All AEs of Suspected, Probable, Confirmed for COVID-19 Infection	T			L
COVID-19 Diagnosis	T			L

NOTES :

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- Individual = Represents FL related to any displays of individual subject observed data.

1. Includes reason for any dose change/interruption in both arms.
2. For AEs reported more than once by a subject, the most severe intensity will be included.
3. One listing of all AEs including verbatim text and preferred term, one showing the relationship between verbatim text, preferred term and SOC and another giving subject numbers for individual all treatment emergent AEs.
4. Common AEs are those with >=2% (or 0.5% for drug-related grade 2-5 AEs if there are no such AEs >=2%) incidence in either treatment group summarised by frequency.
5. Plots of incidence rates and relative risk with 95% CI for DTG/3TC vs. CAR.
6. Four PSRAE listings: Event and Description (Section 1- Section 2), Possible Cause (Section 3), Section 4 and Section 5-Section 8 of the PSRAE eCRF.
7. Repeated by subgroup (see Section 5.4.2).
8. Repeated by maximum grade as well.
9. Incidence of COVID-19 reported as an AE, SAE, treatment discontinuation due to AE of COVID-19 infection will be available in the adverse events summary tables/listings.

8.2. Adverse Events of Special Interest Analyses

A comprehensive list of MedDRA terms based on clinical review will be used to identify each type of event (see Section 15.6.4) . Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting and/or emerging data from on-going studies may highlight additional adverse events of special interest, therefore the list of terms to be used for each event of interest and the specific events of interest will be based on the safety review team (SRT) agreements in place at the time of reporting. An overview of the planned adverse events of special interest analyses are presented in Table 7 and full details of the planned displays are provided in Appendix 16: List of Data Displays.

Table 7 Overview of Planned Adverse Events of Special Interest Analyses

Endpoint	Absolute			
	Summary		Individual	
	T	F	F	L
Adverse Events of Special Interest[1]				
Characteristics of Post Baseline AESI	Y			

1 See Section 15.6.4. for detail list of AESI

8.3. Clinical Laboratory and Biomarker Analyses

Laboratory evaluations will be based on GSK Core Data Standards. Table 8 provides an overview of the planned laboratory analyses, with full details of data displays being presented in Appendix 16: List of Data Displays.

Table 8 Overview of Planned Laboratory Analyses

Endpoint	Absolute				Change from Baseline						Max Post BL			
	Summary		Individual		Summary		Individual		Stats Analysis		Summary		Individual	
	T	F	F	L	T	F	F	L	T	F	T	F	F	L
Laboratory Values Over Time														
Clinical Chemistry[7]	Y			Y[1]	Y									
Fasted Lipid (Triglycerides, LDL, HDL and TC and TC/HDL)[2]	Y[4]		Y[3,4]	Y[1]	Y[4]				Y	Y				
NCEP shifts in lipids					Y[4]	Y[3,4]								
Hematology [7]	Y			Y[1]	Y									
Urine Dipstick				Y[1]										
Urine Concentration				Y[1]										
Liver Chemistries												Y		
Clinical Laboratory and Biomarkers[8]														
Bone Biomarkers				Y	Y			Y	Y	Y				
Renal Biomarkers				Y	Y			Y	Y	Y				
Inflammation Biomarkers				Y	Y			Y	Y	Y				
Change from Baseline in HOMA-IR, HbA1c at Week 24 and 48				Y	Y			Y	Y	Y				
HOMA-IR, HbA1c by visit	Y				Y				Y	Y				
HOMA-IR vs Weight Scatter Plot							Y[5]							
HOMA-IR cut-off (>=2, >=3 and >=4) at Week 24 and 48					Y				Y					
Emergent Laboratory Toxicities														
Clinical Chemistry	Y													
Hematology	Y													
AST, ALT and Total Bilirubin Maximum Post-Baseline Emergent Toxicity by Baseline Hepatitis C Status											Y			

NOTES :

- T = Table, F = Figures, L = Listings, Y = Yes display generated.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

1. Listings for subjects with abnormalities for potential clinical concern/importance, defined as any Grade1-5 toxicity for Chemistry (Including Lipids), Hematology and Urinalysis.
2. Present both mmol/L and mg/DL .
3. Heatmap plot of NCEP categories in lipids over time.
4. Subjects on lipid-lowering agents at baseline are not included in summaries. see Lipids. Section 15.6.4 for more details.
5. A scatter plot of change in HOMA-IR (y-axis) vs change in weight (x-axis) at Weeks 24 and 48.
6. See Section 15.6.4 for more details.
7. Repeated by subgroup
8. Subjects from China will not be evaluated on Inflammatory Biomarkers, telomere length, Bone biomarkers and some Renal biomarkers (Retinol Binding Protein,Beta-2-Microglobulin, Urine RBP/creatinine and Urine B2M/creatinine)

8.3.1. Lipid Parameters Analyses

Statistical Analyses
Endpoints
• Change from Baseline in Fasting Lipids (Triglycerides, LDL cholesterol, HDL cholesterol, Total Cholesterol and TC/HDL ratio) at Weeks 24 and 48
Covariates & Factors
• Baseline 3rd Line Agent • CD4+ cell count (continuous) • Age (continuous) • Sex (Female vs. Male) • Race (White, Black or African American, Asian, Other)
Data Handling
• Before model fitting, missing values are assigned in the Observed Case Dataset: ○ Non-fasting values will be set to missing. ○ Subjects initiated serum lipid-lowering therapy at baseline (see Section 15.6.4) will be excluded from the analysis. ○ All values after initiation of lipid-lowering agents will be set to missing ○ Missing scheduled visits do not need to be created (given all scheduled visits appear in the dataset) ○ Non-missing values will need to be natural logarithm (ln) transformed(including baseline value when included in models) ○ Depending on data structure, transpose non-missing values by subject if necessary
Model Specification
• Multiple imputation technique will be used as described below; ○ Multiple imputations will be drawn from a multivariate normal imputation model (taking into account scheduled measurements prior to analysis timepoints) with a Markov Chain Monte Carlo (MCMC) approach to estimate posterior distributions. The MCMC method in the MI procedure in SAS calling SAS PROC

Statistical Analyses
MI will be used with multiple chains, 500 burn-in iterations, and a noninformative prior. A random seed number of 208090 will be used in the SAS program. Where a subject has a monotone or non-monotone pattern of missingness, all of their missing observations can be imputed under this approach. The absolute value will be imputed before the change value is calculated. Imputations will be drawn separately for subsets of subjects according to their treatment group, i.e., based on means and variance-covariances from the same treatment group (Missing At Random (MAR) approach) conditioning on covariates (as defined above). ○ The imputations will be carried out 1,000 times. An ANCOVA (Week 24)/ MMRM (Week 48), using the observed margins (OM) option, will be performed on each dataset produced adjusting for the covariates (listed above), treatment, and baseline value, regardless of their significance. PROC MI ANALYZE in SAS will be used to combine the 1,000 estimated least squares means and difference to produce one estimated mean with 95% CI and associated p-value for the adjusted mean difference between each treatment group at Week 24 and Week 48. ○ Interactions between treatment and covariates will not be assessed.
Model Checking & Diagnostics
Refer to Appendix 14: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Given that data is log transformed, estimated adjusted ratio (Week 24/Baseline or Week 48/Baseline) for each treatment and geometric mean ratio ((DTG/3TC/ CAR)) together with corresponding 95% CI will be presented. Results of the ratio are also expressed as percent change in adjusted mean and percent treatment difference respectively where percent change is derived as 100* [Exp(model parameter estimate) -1].
Sensitivity Analyses - ANCOVA (Week 24)
• Sensitivity Analysis with Analysis of Covariance (ANCOVA) will be performed on the original data without multiple imputation techniques to deal with the missing data. • ANCOVA will use the observed margins (OM) option, adjusting for treatment, covariates (listed above) and baseline value. • Type III tests for the least-squares (LS) means will be used for the statistical comparison; the 95% CI will also be reported. Treatment group comparisons at Week 24 will be reported. • Adjusted least squares means and corresponding standard errors (SEs) of adjusted least squares means will be presented for each treatment, together with estimated treatment difference (DTG/3TC – CAR) and corresponding 95% confidence interval and p-value. • Note: if any lipid parameter is not normally distributed then the geometric mean and a 95% CI of geometric mean will be presented for each treatment, as well as geometric mean ratios and corresponding 95% CI and a p-value.

Statistical Analyses
Sensitivity Analyses – MMRM(Week 48)
• Sensitivity Analysis with Mixed Model Repeated Measures (MMRM) will be performed on the original data without multiple imputation techniques to deal with the missing data. • MMRM will use the observed margins (OM) option, adjusting for treatment, covariates (listed above) and baseline value, with visit as the repeated factor. • The model will make no further assumptions about the correlations within-subject scores (the correlation matrix for within-subject errors will be unstructured). • The repeated measures analysis will assume that the treatment difference can vary between visits (i.e.. a treatment*visit interaction will be included in the model). The model will also assume that the effect of baseline score for the endpoint can vary between visits (i.e.. baseline score*visit interaction will be included in the model). • The Kenward-Roger method will be used to estimate the denominator degrees of freedom. Type III tests for the least-squares (LS) means will be used for the statistical comparison; the 95% CI will also be reported. Treatment group comparisons at Week 24 and Week 48 will be reported. • Adjusted least squares means and corresponding standard errors (SEs) of adjusted least squares means will be presented for each treatment, together with estimated treatment difference (DTG/3TC – CAR) and corresponding 95% confidence interval and p-value. • Note: if any lipid parameter is not normally distributed then the geometric mean and a 95% CI of geometric mean will be presented for each treatment, as well as geometric mean ratios and corresponding 95% CI and a p-value.

8.3.2. HOMA-IR and HbA1c Analyses

Statistical Analyses
Endpoints
• Change from baseline in HOMA-IR, HbA1c at Weeks 24 and 48 (refer to 15.6.4 for details of derivation)
Covariates & Factors
• Baseline 3rd Line Agent • CD4+ cell count (continuous) • Age (continuous) • Sex (Female vs. Male) • Race (White, Black or African American, Asian, Other) • BMI (continuous) • Presence of diabetes mellitus (DM) (Yes vs no) : Applicable for HbA1c only • Hypertension (Yes vs no) • Baseline value(continuous)
Data Handling
• No multiple imputation techniques will be used to deal with the missing data.

Statistical Analyses
Model Specification
• If change in HOMA-IR or HbA1c is not normally distributed the data will be log transformed and geometric means will replace arithmetic means, a 95% CI will replace the standard deviations and mean changes from baseline will be presented as geometric mean ratios. • Change from baseline will be analysed for the comparison between DTG/3TC and CAR. • Using OC dataset, the Mixed Model Repeated Measures (MMRM), using the observed margins (OM) option, will adjust for treatment, covariates (listed above) and baseline value as a covariate, with visit as the repeated factor. • The model will make no further assumptions about the correlations between a subject's value (the correlation matrix for within-subject errors will be unstructured). • The repeated measures analysis will assume that the treatment difference can vary between visits (i.e. a treatment*visit interaction will be included in the model), and separate estimates and 95% confidence intervals will be produced at each visit. The model will also assume that the effect of baseline value for the endpoint can vary between visits (i.e. baseline value*visit interaction will be included in the model). • Interactions between treatment and each of the covariates will not be assessed.
Model Checking & Diagnostics
• Refer to Appendix 14: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Adjusted least squares means and corresponding standard errors (SEs) of adjusted least squares means will be presented for each treatment, together with estimated treatment difference (DTG/3TC – CAR) and corresponding 95% confidence interval and p-value. • Note: If change from baseline in HOMA-IR or HbA1c data are not normally distributed, the geometric mean and a 95% CI of geometric mean will be presented for each treatment, as well as geometric mean ratios and corresponding 95% CI and a p-value.
Sensitivity Analyses
• Line plots of LS means with 95% confidence intervals for Adjusted Mean Change from Baseline will be generated for each treatment group by visit • A logistic regression model will be performed on the proportion of subjects with HOMA-IR cut-off (>=2, >=3 and >=4) at Week 24 and Week 48 adjusting for the same covariates as specified in the MMRM analysis (without visit or interaction terms). Odds ratios, standard errors, confidence intervals and p-values will be presented for all covariates specified in the model. This analysis will be repeated on the proportion of subjects with HOMA-IR cut-off (>=2, >=3 and >=4) at Week 24 and Week 48. Upon delivery of data, an assessment regarding the amount of missing data will be made. If it's considered the amount of missing HOMA-IR outcome data at Week 24 and Week 48 as a result of COVID-19 is substantial, the logistic regression analysis may not be performed.
Subgroup Analyses
• Not applicable

8.3.3. Bone Biomarkers Analyses

Statistical Analyses
Endpoints
• Change from baseline in bone biomarkers (bone specific alkaline phosphatase, procollagen type I N-terminal propeptide, type I collagen cross-linked C-telopeptide, osteocalcin) at Weeks 24 and 48
Covariates & Factors
• Baseline 3rd Line Agent • CD4+ cell count (continuous) • Age (continuous) • Sex (Female vs. Male) • Race (White, Black or African American, Asian, Other) • BMI (continuous) • Smoking status (Never vs. Former vs. Current Smoker) • Baseline value(continuous)
Data Handling
• No multiple imputation techniques will be used to deal with the missing data.
Model Specification - ANCOVA (Week 24)
• It is anticipated that at least some biomarkers will not be normally distributed and for those, the data will be log transformed and geometric means will replace arithmetic means, a 95% CI will replace the standard deviations and mean changes from baseline will be presented as geometric mean ratios. • Change from baseline will be analysed for each bone biomarker for the comparison between DTG/3TC and CAR. • An Analysis of Covariance (ANCOVA), using the observed margins (OM) option, will adjust for treatment, covariates (listed above) and biomarker value at baseline as a covariate. The OC dataset will be used for ANCOVA model.
Model Specification – MMRM (Week 48)
• It is anticipated that at least some biomarkers will not be normally distributed and for those, the data will be log transformed and geometric means will replace arithmetic means, a 95% CI will replace the standard deviations and mean changes from baseline will be presented as geometric mean ratios. • Change from baseline will be analysed for each bone biomarker for the comparison between DTG/3TC and CAR. • Mixed Model Repeated Measures (MMRM), using the observed margins (OM) option, will adjust for treatment, covariates (listed above) and biomarker value at baseline as a covariate, with visit as the repeated factor. The OC dataset will be used for MMRM model. • The model will make no further assumptions about the correlations between a subject's value (the correlation matrix for within-subject errors will be unstructured). • The repeated measures analysis will assume that the treatment difference can vary between visits (i.e. a treatment*visit interaction will be included in the model) and separates estimates and 95% confidence intervals will be produced at each visit. The model will also assume that the effect of baseline value for the endpoint can vary between visits (i.e. baseline value*visit interaction will be included in the model). • Interactions between treatment and each of the covariates will not be assessed.

Statistical Analyses
Model Checking & Diagnostics
• Refer to Appendix 14: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Adjusted least squares means and corresponding standard errors (SEs) of adjusted least squares means will be presented for each treatment, together with estimated treatment difference (DTG/3TC – CAR) and corresponding 95% confidence interval and p-value. • Note: For biomarkers that are not normally distributed, the geometric mean and a 95% CI of geometric mean will be presented for each treatment, as well as geometric mean ratios and corresponding 95% CI and a p-value.
Sensitivity Analyses
• Line plots of LS means with 95% confidence intervals for Adjusted Mean Change from Baseline will be generated for each treatment group by visit
Subgroup Analyses
• Not applicable

8.3.4. Renal Biomarkers Analyses

Statistical Analyses
Endpoints
• Change from baseline in renal biomarkers (serum Cystatin C, Urine Beta-2 Microglobulin /Urine Creatinine ratio (mg/mmol), urine albumin/creatinine ratio, urine protein/creatinine ratio, urine phosphate, eGFR (based on CKD-EPI-creatinine and CKD-EPI-cystatin C), serum creatinine and Urine Retinol Binding Protein 4/Urine Creatinine ratio (ug/mmol)) at Weeks 24 and 48
Covariates & Factors
• Baseline 3rd Line Agent • CD4+ cell count (continuous) • Age (continuous) • Sex (Female vs. Male) • Race (White, Black or African American, Asian, Other) • BMI (continuous) • Presence of diabetes mellitus (DM) (Yes vs no) • Presence of Hypertension (Yes v no) • Baseline value(continuous)
Data Handling
• No multiple imputation techniques will be used to deal with the missing data.
Model Specification - ANCOVA (Week 24)
• It is anticipated that at least some biomarkers will not be normally distributed and for those, the data will be log transformed and geometric means will replace arithmetic means, a 95% CI will replace the standard deviations and mean changes from baseline will be presented as geometric mean ratios. • Change from baseline will be analysed for each bone biomarker for the comparison between DTG/3TC and CAR.

Statistical Analyses
• An Analysis of Covariance (ANCOVA), using the observed margins (OM) option, will adjust for treatment, covariates (listed above) and biomarker value at baseline as a covariate. The OC dataset will be used for ANCOVA model.
Model Specification – MMRM (Week 48)
• It is anticipated that at least some biomarkers will not be normally distributed and for those, the data will be log transformed and geometric means will replace arithmetic means, a 95% CI will replace the standard deviations and mean changes from baseline will be presented as geometric mean ratios. • Change from baseline will be analysed for each renal biomarker for the comparison between DTG/3TC and CAR. • Using OC dataset, the Mixed Model Repeated Measures (MMRM), using the observed margins (OM) option, will adjust for treatment, covariates (listed above) and baseline renal biomarker value at baseline as a covariate, with visit as the repeated factor. • The model will make no further assumptions about the correlations between a subject's value (the correlation matrix for within-subject errors will be unstructured). • The repeated measures analysis will assume that the treatment difference can vary between visits (i.e. a treatment*visit interaction will be included in the model), and separate estimates and 95% confidence intervals will be produced at each visit. The model will also assume that the effect of baseline value for the endpoint can vary between visits (i.e. baseline value*visit interaction will be included in the model). • Interactions between treatment and each of the covariates will not be assessed.
Model Checking & Diagnostics
• Refer to Appendix 14: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Adjusted least squares means and corresponding standard errors (SEs) of adjusted least squares means will be presented for each treatment, together with estimated treatment difference (DTG/3TC – CAR) and corresponding 95% confidence interval and p-value. • Note: For biomarkers that are not normally distributed, the geometric mean and a 95% CI of geometric mean will be presented for each treatment, as well as geometric mean ratios and corresponding 95% CI and a p-value.
Sensitivity Analyses
• Line plots of LS means with 95% confidence intervals for Adjusted Mean Change from Baseline will be generated for each treatment group by visit • A sensitivity analysis will be performed for urine albumin/creatinine ratio and urine protein/creatinine ratio by imputing albumin, protein and creatinine values that are below the limit of quantitation. See Appendix 7.
Subgroup Analyses
• Not applicable

8.3.5. Inflammatory Biomarkers Analyses

Statistical Analyses
Endpoints
• Change from baseline in inflammatory biomarkers (Interleukin-6 (IL-6), High-sensitivity C reactive protein (hs-CRP), D-dimer, Soluble CD14 (sCD14), Soluble CD163 (sCD163)) at Weeks 24 and 48
Covariates & Factors
• Baseline 3rd Line Agent • CD4+ cell count (continuous) • Age (continuous) • Sex (Female vs. Male) • Race (White, Black or African American, Asian, Other) • BMI (continuous) • Smoking status (Never vs. Former vs. Current Smoker) • HCV-coinfection (Yes vs. No) • Baseline value(continuous)
Data Handling
• No multiple imputation techniques will be used to deal with the missing data.
Model Specification - ANCOVA (Week 24)
• It is anticipated that at least some biomarkers will not be normally distributed and for those, the data will be log transformed and geometric means will replace arithmetic means, a 95% CI will replace the standard deviations and mean changes from baseline will be presented as geometric mean ratios. • Change from baseline will be analysed for each bone biomarker for the comparison between DTG/3TC and CAR. • An Analysis of Covariance (ANCOVA), using the observed margins (OM) option, will adjust for treatment, covariates (listed above) and biomarker value at baseline as a covariate. The OC dataset will be used for ANCOVA model.
Model Specification – MMRM (Week 48)
• It is anticipated that at least some biomarkers will not be normally distributed and for those, the data will be log transformed and geometric means will replace arithmetic means, a 95% CI will replace the standard deviations and mean changes from baseline will be presented as geometric mean ratios. • Change from baseline will be analysed for each inflammatory biomarker for the comparison between DTG/3TC and CAR. • Using OC dataset, the Mixed Model Repeated Measures (MMRM), using the observed margins (OM) option, will adjust for treatment, covariates (listed above) and baseline inflammatory biomarker value at as a covariate, with visit as the repeated factor. • The model will make no further assumptions about the correlations between a subject's value (the correlation matrix for within-subject errors will be unstructured). • The repeated measures analysis will assume that the treatment difference can vary between visits (i.e. a treatment*visit interaction will be included in the model), and separate estimates and 95% confidence intervals will be produced at each visit. The model will also assume that

Statistical Analyses
the effect of baseline value for the endpoint can vary between visits (i.e. baseline value*visit interaction will be included in the model). • Interactions between treatment and each of the covariates will not be assessed.
Model Checking & Diagnostics
• Refer to Appendix 14: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Adjusted least squares means and corresponding standard errors (SEs) of adjusted least squares means will be presented for each treatment, together with estimated treatment difference (DTG/3TC – CAR) and corresponding 95% confidence interval and p-value. • Note: For biomarkers that are not normally distributed, the geometric mean and a 95% CI of geometric mean will be presented for each treatment, as well as geometric mean ratios and corresponding 95% CI and a p-value.
Sensitivity Analyses
• Line plots of LS means with 95% confidence intervals for Adjusted Mean Change from Baseline will be generated for each treatment group by visit
Subgroup Analyses
• Not applicable

8.4. Other Safety Analyses

The analyses of non-laboratory safety test results will be based on GSK Core Data Standards, unless otherwise specified. An overview of other safety analyses is presented in Table 9 and full details of the planned displays are presented in Appendix 16: List of Data Displays. Note that ECGs and vital signs are only collected at screening, so will only be listed.

Table 9 Overview of Other Safety Analyses

Endpoint	Absolute				Change from Baseline						Max Post BL			
	Summary		Individual		Summary		Individual		Stats Analysis		Summary		Individual	
	T	F	F	L	T	F	F	L	T	F	T	F	F	L
Other Safety Analyses														
ECG at screening				Y										
Vital Signs				Y										
Liver Assessment	Y			Y										
Hepatobiliary Abnormality criteria	Y			Y[3]										
eC-SSRS	Y			Y[1]										
Subjects who became Pregnant				Y										
Patient Profiles				Y[2]										

Endpoint	Absolute				Change from Baseline						Max Post BL			
	Summary		Individual		Summary		Individual		Stats Analysis		Summary		Individual	
	T	F	F	L	T	F	F	L	T	F	T	F	F	L
Pharmacokinetics Listings for Subjects with Liver Stopping Events				Y										
Weight and BMI														
Change from baseline in BMI at Weight at Week 24 and 48				Y	Y			Y	Y	Y				
BMI[4] and Weight by Visit	Y				Y				Y	Y				
BMI shift Table	Y													

1. Includes Baseline and lists all visits for a subject who reports any ideation or behaviour at any visit.
2. Patient profiles for subjects meeting protocol defined liver stopping criteria and for patients with HIV-1 RNA ≥ 50 c/mL. Patient profiles can also be provided for any other subjects.
3. All post-baseline abnormalities meeting Hepatobiliary Abnormality Criteria.
4. Heatmap plot of BMI categories over time.

8.4.1. Weight and BMI Analyses

Statistical Analyses
Endpoints
• Change from baseline in weight (kg) and BMI (kg/m2) at Weeks 24 and 48
Covariates & Factors
• Baseline 3rd Line Agent • CD4+ cell count (continuous) • Age (continuous) • Sex (Female vs. Male) • Race (White, Black or African American, Asian, Other) • Baseline value(continuous)
Data Handling
• No multiple imputation techniques will be used to deal with the missing data.
Model Specification
• If the change from baseline in weight (BMI for BMI analysis) is not normally distributed, the data will be log transformed and geometric means will replace arithmetic means, a 95% CI will replace the standard deviations and mean changes from baseline will be presented as geometric mean ratios. • Change from baseline will be analysed for the comparison between DTG/3TC and CAR. • Using OC dataset, the Mixed Model Repeated Measures (MMRM), using the observed margins (OM) option, will adjust for treatment, covariates (listed above) and baseline weight (BMI for BMI analysis) value as a covariate, with visit as the repeated factor.

Statistical Analyses
• The model will make no further assumptions about the correlations between a subject's weight (BMI for BMI analysis) (the correlation matrix for within-subject errors will be unstructured). • The repeated measures analysis will assume that the treatment difference can vary between visits (i.e. a treatment*visit interaction will be included in the model), and separate estimates and 95% confidence intervals will be produced at each visit. The model will also assume that the effect of baseline weight (BMI for BMI analysis) can vary between visits (i.e. baseline value*visit interaction will be included in the model). • Interactions between treatment and each of the covariates will not be assessed.
Model Checking & Diagnostics
• Refer to Appendix 14: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Adjusted least squares means and corresponding standard errors (SEs) of adjusted least squares means will be presented for each treatment, together with estimated treatment difference (DTG/3TC – CAR) and corresponding 95% confidence interval. • Note: If change in weight is not normally distributed, the geometric mean and a 95% CI of geometric mean will be presented for each treatment, as well as geometric mean ratios and corresponding 95% CI and p-values.
Sensitivity Analyses
• Line plots of LS means with 95% confidence intervals for Adjusted Mean Change from Baseline will be generated for each treatment group by visit.
Subgroup Analyses
• Not applicable

9. OTHER STATISTICAL ANALYSES

9.1. Health Outcomes

9.1.1. Overview of Planned Analyses

The Health Outcomes analyses will be based on the Intent-To-Treat (Exposed) population, unless otherwise specified.

Table 10 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 16: List of Data Displays.

Table 10 Overview of Planned Health Outcome Analyses

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Symptom Distress Module (SDM)														
Symptom Count (at Week 24 and 48)				Y			Y				Y			
Symptom Bother Score (at Week 24 and 48)				Y			Y	Y[3]	Y[1]		Y			
Willingness to switch														
Willingness to switch survey				Y										
Treatment satisfaction														
HIVTSQ individual item scores by Visit				Y			Y							
HIVTSQ (at Week 24 and 48)	Y[2]			Y[2]				Y[2,3]	Y[1,2]		Y[2]			

1. Line Plot of Adjusted Mean (95% CI) and Line Plot of Difference (95% CI) in Adjusted Mean Change from Baseline over time.
2. Separate summaries for Total score (questionnaire items 1-10), General Satisfaction/Clinical sub-score (questionnaire items [redacted] and [redacted] and Lifestyle/ease sub-score (questionnaire items [redacted] and [redacted].
3. Repeat by subgroups (see Section 5.4.2).

9.1.2. Planned Health Outcomes Statistical Analyses

Statistical Analyses
Endpoints
• Change from baseline in Overall Symptom Bother score at Week 24 and 48 • Change from baseline in HIVTSQ total score at Week 24 and 48 • Change from baseline in HIVTSQ general satisfaction/clinical sub-score at Week 24 and 48 • Change from baseline in HIVTSQ lifestyle/ease sub-scores at Week 24 and 48

Covariates & Factors
• Baseline 3rd Line Agent • Age (continuous) • Sex (Female vs. Male) • Race (White, Black or African American, Asian, Other) • Baseline score
Data Handling
• No multiple imputation techniques will be used to deal with the missing data.
Model Specification
• If the endpoint is not be normally distributed then, the data will be log transformed and geometric means will replace arithmetic means, a 95% CI will replace the standard deviations and mean changes from baseline will be presented as geometric mean ratios. • Change from baseline will be analysed for the comparison between DTG/3TC and CAR • Using OC dataset, Mixed Model Repeated Measures (MMRM), using the observed margins (OM) option, will adjust for treatment, covariates (listed above) and baseline score value as a covariate, with visit as the repeated factor. • The model will make no further assumptions about the correlations between a subject's score (the correlation matrix for within-subject errors will be unstructured). • The repeated measures analysis will assume that the treatment difference can vary between visits (i.e. a treatment*visit interaction will be included in the model) and separates estimates and 95% confidence intervals will be produced at each visit. The model will also assume that the effect of baseline score for the endpoint can vary between visits (i.e. baseline score*visit interaction will be included in the model). • Interactions between treatment and each of the covariates will not be assessed.
Model Checking & Diagnostics
• Refer to Appendix 14: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Adjusted least squares means and corresponding standard errors (SEs) of adjusted least squares means will be presented for each treatment, together with estimated treatment difference (DTG/3TC – CAR) and corresponding 95% confidence interval and p-value. • Note: if SDM bother score is not normally distributed, the geometric mean and a 95% CI of geometric mean will be presented for each treatment, as well as geometric mean ratios and corresponding 95% CI and a p-value.
Sensitivity Analyses
• Line plots of LS means with 95% confidence intervals for Adjusted Mean Change from Baseline will be generated for each treatment group by visit
Subgroup Analyses
• Subgroup analyses will be performed for change from baseline in Overall Symptom Bother score and HIVTSQ total score at Week 24 and 48. Analysis will be performed as described above and will adjust for the covariates listed above, treatment, baseline score, subgroup, baseline score*visit and treatment*subgroup interaction term regardless of their significance (Subgroups are defined in Section 5.4.2).

Statistical Analyses
Endpoint(s)
• Willingness to switch survey
Model Specification/Analysis Methodology
• Assess the reason(s) for their participation and facilitate an understanding of subject's willingness to switch • A single item question prior to randomisation. • 7 reasons for willingness to participate in a clinical study where the current HIV medication may be switched check all that apply • Any missing values will remain missing
Model Results Presentation
• Summary statistics will be presented by treatment group

9.2. Virology

9.2.1. Overview of Planned Analyses

9.2.2. Planned Virology Statistical Analysis

The virology analyses of genotype and phenotype data will be based on the CVW and pPVW resistance populations. Please see Section 15.6.3 for details of the derivation of CVW. Please see Section 15.6.3 for details of the derivation of pPVW.

The CVW population will be based on subjects who have experienced a CVW at any point. Summary tables will present CVWs up to and including the time point of interest. CVWs must be confirmed within the phase in which they are reported. Listings will present CVWs occurring at any point. Summary tables will present CVWs at the time point of SVW (or first elevation if this was >=50 c/mL and <200 c/mL).'

Table 11 provides an overview of the planned virology analyses, with full details of data displays being presented in Appendix 16: List of Data Displays.

Table 11 Overview of Planned Virology Analyses

Endpoint	Absolute			
	Summary		Individual	
	T	F	F	L
HIV-1 Subject Genotypic/Phenotypic Data Accountability				
Genotypic Accountability	Y[2]			
Phenotypic Accountability	Y[2]			
Genotypic resistance				
Genotypic resistance at time of CVW[1]	Y[2]			Y[4]
Genotypic resistance for subjects on treatment non-CVW time point[1]	Y[2]			Y
Phenotypic resistance[5]				
Phenotypic resistance at time of CVW[1]	Y[3]			Y[4]

Endpoint	Absolute			
	Summary		Individual	
	T	F	F	L
Phenotypic resistance for subjects on treatment at non-CVW time point[1]	Y[2]			Y
INI and RT/PR replication capacity at time of CVW[1]				Y[4]
INI and RT/PR replication capacity at time of non-CVW[1]				Y[4]
Fold Change at CVW	Y			
Net Assessment for Overall Susceptibility Score				
Overall Susceptibility Score (OSS)				Y

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

1. Sample used for resistance testing is taken at the time suspected virologic withdrawal criteria are met, and only tested once virologic withdrawal criteria are confirmed at a subsequent visit.
2. Separate outputs for INI and NRTI/NNRTI/PI mutations
3. Separate outputs by phenotypic cut-off and by number of drugs to which subjects are resistant.
4. Produce for CVW and pPVW resistance populations.
5. Phenotypic data are not available at Baseline because Genosure archive assay being used only provides genotype and not phenotype

10. PHARMACOKINETIC ANALYSES

There are no pharmacokinetic analyses planned for this study.

11. POPULATION PHARMACOKINETIC (POPPK) ANALYSES

There are no population pharmacokinetic analyses planned in this study.

12. PHARMACODYNAMIC ANALYSES

There are no pharmacodynamic analyses planned for this study.

13. PHARMACOKINETIC / PHARMACODYNAMIC ANALYSES

There are no pharmacokinetic / pharmacodynamic (PK/PD) analyses planned in this study.

14. REFERENCES

D'Agostino R.B., Vasan R.S., Pencina M.J., Wolf P.A., Cobain M., Massaro J.M. Kannel W.B. General Cardiovascular Risk Profile for Use in Primary Care: The Framingham Heart Study. *Epidemiology*. 2008; 117:743-753.

Fleiss J.L. *Statistical Methods for Rates and Proportions.* 2nd ed. New York:John Wiley; 1981.

Grundy S.M., et al. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA*. 2001;285

Inker LA, Schmid CH, Tighiouart H, et al; Estimating Glomerular Filtration Rate from Serum Creatinine and Cystatin C. *N Engl J Med*. 2012;367:20-9.

Johnson VA, Calvez V, Gunthard HF, et. al. Special Contribution. Update of the Drug Resistance Mutations in HIV-1: March 2013. IAS-USA Topics in Antiviral Medicine. Available at: https://www.iasusa.org/sites/default/files/tam/21-1-6.pdf. Accessed Octover 24, 2016.

Justice A, Holmes W, Gifford A, et al. Development and validation of a self completed HIV symptom index. Journal of Clinical Epidemiology. 2001; 54:S77-S90

Kalbfleisch JD, Prentice RL. The Statistical Analysis of Failure Time Data. *New York: Wiley,* 1980

Klingenberg. A new and improved confidence interval for the Mantel-Haenszel risk difference. *Statistics in Medicine*. 2014; 2968-2983.

Levey AS, Stevens LA, Schmid CH, et.al. A new equation to estimate glomerular filtration rate. *Ann Int Med*. 2009;150:604-12.

Liu TF, Shafer RW. Web Resources for HIV type 1 Genotypic-Resistance Test Interpretation. *Clin Infect Dis*. 2006;42 (11):1608-1618.

Lui K.J., Kelly C. A Revisit on Tests for Homogeneity of the Risk Difference, *Biometrics*, 2000;56:309-315.

Miettinen O, Nurminen M. Comparative Analysis of two rates. *Statistics in Medicine*. 1985; 4:213-226.

Posner K, Oquendo MA, Gould M, Stanley B, Davies M. Columbia Classification Algorithm of Suicide Assessment (C-CASA): classification of suicidal events in the FDA's pediatric suicidal risk analysis of antidepressants. *Am J Psychiatry*. 2007;164:1035–43.

Sato T. On the variance estimator for the Mantel-Haenszel risk difference. *Biometrics.* 1989;42:311-323.

Woodcock A, Bradley C . Validation of the HIV treatment satisfaction questionnaire (HIVTSQ). Qual Life Res. 2001;10(6):517-531.

Woodcock A, Bradley C. Validation of the revised 10-item HIV Treatment Satisfaction Questionnaire status version and new change version. Value Health. 2006;9(5):320-333.

15. APPENDICES

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Section 15.17	Appendix 17: Example Mock Shells for Data Displays

15.1. Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population

15.1.1. Exclusions from Per Protocol Population

A subject meeting any of the following criteria (Significant Protocol Deviations) will be excluded from the Per Protocol population:

Number	Exclusion criteria
01	Subject deviates from any inclusion or exclusion criteria, as recorded in the eCRF
02*	Subject took/received incorrect IP, i.e., other than the one to which they were randomized for greater than 10% of the total time On-treatment
03*	Interruption of IP for greater than 10% of the total time On-treatment, for reasons other than treatment-related adverse events/laboratory abnormalities, based on eCRF IP exposure forms or eCRF CONMEDS forms in case commercial supply is used before study completion.
04	HIV immunotherapeutic vaccines used
05	Concurrent use of drugs that may decrease DTG concentration for >7 days: (Carbamazepine, Oxycarbamazapine, Phenobarbital, Phenytoin, St. John's wort (Hypericum perforatum), rifampin
06	Concomitant use of rifapentin
07	Other experimental agents, antiretroviral drugs not otherwise specified in the protocol, cytotoxic chemotherapy, or radiation therapy used
08	Systemically administered immunomodulators used through Week 48 visit
09	HCV therapy based on interferon or any other medications that have a potential for adverse drug-drug interactions with study treatment

10	Concomitant use of acetaminophen in subjects with acute viral hepatitis
11	Dofetilide or pilsicainide used concurrently with DTG
12	Subject's change (i.e., substitution or dose modification) of DTG, 3TC or component of CAR (except protocol allowed switches, e.g. switch of booster) but was not withdrawn from the study
13	Subject became pregnant while on study
14	Permanent discontinuation of IP/withdrawal due to a reason of “Protocol Deviation” (as recorded in the eCRF)

*Programmatically derived protocol deviations (PD), which are defined in a separate protocol deviations specification document. Please refer to Section 15.6.7 regarding cut-off dates regarding protocol deviations leading to exclusion from the per protocol set.

15.2. Appendix 2: Schedule of Activities

15.2.1. Protocol Defined Schedule of Events

Procedures	Screening Visit[a]	Randomized Phase							Continuation Phase[c]	Withdrawal	Follow-up[d]
		Baseline/ Day 1	4	12	24	36	48[b]	52	Every 12 Weeks After Week 52		
Clinical and Other Assessments											
Written informed consent	X										
Inclusion/Exclusion criteria[e]	X	X									
Demography	X										
Prior ART history	X										
Medical history[f]	X										
Menopause history[g]	X	X						X		X	
Current medical conditions	X										
Cardiovascular risk assessment including vital signs[h]	X										
Body Weight (BMI will be calculated within the eCRF)[i]	X	X	X	X	X	X	X	X	X	X	X
HIV risk factors and mode of transmission		X									
CDC HIV-1 classification	X	X									
HIV associated conditions[j]		X	X	X	X	X	X	X	X	X	
Columbia Suicidality Severity Rating Scale		X[k]	X	X	X	X	X	X	X	X	
Concomitant medication	X	X	X	X	X	X	X	X	X	X	X
Symptom Directed Physical Exam[l]	X	X	X	X	X	X	X		X	X	X

Procedures	Screening Visit[a]	Randomized Phase							Continuation Phase[c]	Withdrawal	Follow-up[d]
		Baseline/ Day 1	4	12	24	36	48[b]	52	Every 12 Weeks After Week 52		
12-lead ECG[m]	X										
Adverse events		X	X	X	X	X	X	X	X	X	X
Serious adverse events	X[n]	X	X	X	X	X	X	X	X	X	X
Willingness to Switch[o]		X[o]									
HIV TSQ[p]		X	X		X		X			X	
Symptom Distress Module[p]		X	X		X		X		X (every 24 weeks)	X	
Laboratory Assessments											
Quantitative plasma HIV-1 RNA[q]	X	X	X	X	X	X	X		X	X	
Lymphocyte subset[r]	X	X	X	X	X	X	X			X	
Plasma for storage[s]	X	X	X	X	X	X	X		X	X	
Clinical chemistry[t]	X	X	X	X	X	X	X			X	X
Hematology	X	X	X	X	X	X	X			X	X
PT/INR (for Child-Pugh)	X										
Fasting lipids and glucose[u]		X			X		X			X[v]	
Urinalysis and spot urine for protein analysis[w]		X			X		X			X	X
Pregnancy test[x, y]	S	U/S[z]	S	S	S	S	S	S	S	S	
HBsAg, anti-HBc, Anti-HBs, and HBV DNA[aa]	X										
HCV antibody	X										
RPR	X										

Procedures	Screening Visit[a]	Randomized Phase							Continuation Phase[c]	Withdrawal	Follow-up[d]
		Baseline/ Day 1	4	12	24	36	48[b]	52	Every 12 Weeks After Week 52		
Renal, bone and inflammatory marker analytes (blood/urine) and HbA1c, insulin and glucose[bb]		X			X		X			X	
Whole Blood (Virology)[cc]		X					X			X	
Whole Blood (Telomere Length)[dd]		X					X			X[ee]	
PBMCs[ff]		X			X		X			X[gg]	
Study Treatment											
IVRS/IWRS[hh]	X	X	X	X	X	X	X	X	X	X	X
Dispense IP		X	X	X	X	X	X	X	X		
IP accountability (pill counts)			X	X	X	X	X		X	X	

ART - antiretroviral therapy, BMI - body mass index, CDC - centers for disease control and prevention, DNA - deoxyribonucleic acid, ECG – electrocardiogram, eCRF - electronic case report form, HBV – hepatitis B virus, HCV – hepatitis C virus, INR - international normalized ratio, IP - investigational product

a. As soon as all Screening results are available, randomization may occur.
b. Participants with plasma HIV-1 RNA ≥50 c/mL at Week 48 (primary endpoint) must have HIV-1 RNA level re-assessed by a second measurement performed 2-4 weeks later, occurring prior to Week 52.
c. All participants on the DTG/3TC FDC arm who complete through Week 52 will have the opportunity to enter the Continuation Phase. The Continuation Phase is not applicable for participants in Sweden and Denmark. For participants who will not continue past Week 52, do not dispense study intervention. Participants completing the Continuation Phase must return to the clinic for an End of Continuation Phase visit when transitioning to commercial supplies or to an alternate ART regimen, if appropriate. At this visit, conduct study assessments as specified for all Continuation Phase visits except for dispensing study intervention.
d. An in-clinic Follow-Up visit will be conducted 4 weeks after the last dose of study intervention for participants with the following conditions at the last on-study visit: ongoing AEs, serious adverse events (SAEs) regardless of attributability, and any laboratory abnormalities that are considered to be AEs or potentially harmful to the participant. However, the investigator, in consultation with the medical monitor, should follow-up with the participant until the event is resolved, stabilized, otherwise explained, or the participant is lost to follow-up

e. Inclusion/exclusion criteria will be assessed fully at the Screening visit. Changes between the Screening visit and the Day 1 visit should be considered to ensure eligibility, including review of additional assessments performed at Day 1. Genotypic resistance testing results if available MUST be provided to ViiV after screening and before randomization.
f. Full medical history will be conducted prior to randomization and include assessments of cardiovascular, metabolic (e.g., Type I or II diabetes mellitus), psychiatric (e.g., depression), renal (e.g., nephrolithiasis, nephropathy, renal failure), and bone disorders.
g. Menopause history will include date of last menstrual period (collected at Day 1, Week 52 or withdrawal) and menopausal status (collected at Screening, Week 52 or withdrawal) based on the criteria in the Protocol Section 11.4.1. A postmenopausal state is defined as no menses for 12 months without an alternative medical cause.
h. Assessment for cardiovascular risk will include height, weight, blood pressure, smoking status and history, pertinent medical conditions (e.g., hypertension, diabetes mellitus), and family history of premature cardiovascular disease. BMI will be calculated within the eCRF.
i. The same scale should be used to measure body weight at each visit.
j. Based on the participant's current CDC status in the past 6 months.
k. On Day 1, the electronic Columbia Suicidality Severity Rating Scale (eC-SSRS), participant completed questionnaire is to be administered prior to the first dose.
l. Limited physical examination to include blood pressure at Day 1 (recorded in eCRF) for Framingham score assessment. Blood pressure to be measured after resting in a semi-supine position for at least 5 minutes.
m. A 12-lead ECG will be performed in a semi-supine position after resting for at least 5 minutes.
n. Only SAEs related to study participation or to a concomitantly administered ViiV/GSK product will be collected between obtaining informed consent and administration of study intervention at Day 1.
o. Willingness to Switch Survey must be done prior to randomization.
p. Questionnaire/Surveys are recommended to be administered at the beginning of the visit before any other assessments are conducted. Only conduct questionnaires/surveys at Withdrawal if occurring prior to Week 48, except the Symptom Distress Module which should also be collected if Withdrawal occurs during the Continuation Phase.
q. See Virologic Withdrawal and Stopping Criteria Section of protocol (Section 7.1.1).
r. Lymphocyte subset will include collection of CD4 and CD8 for calculation of Cd4:CD8 ratio. CD8 will also be reported to sponsor.
s. Plasma samples for storage will be collected at each visit starting at Day 1, including unscheduled visits (e.g. for HIV-1 RNA levels and immunological parameters). These samples will be used when needed such as when samples are lost, arrive at the laboratory unevaluable, or for genotypic and/or phenotypic analyses when participants meet Suspected and Confirmed Virologic Withdrawal criteria.
t. See Protocol Appendix 7 for a list of clinical chemistry labs.
u. An overnight fast is preferred; however, a minimum of a 6-hour fast is acceptable.
v. Collect fasting lipids and glucose if the Withdrawal visit occurs at Weeks 24 or 48.
w. A morning specimen is preferred. To assess renal biomarkers: urine albumin/creatinine ratio; urine protein/creatinine ratio; and urine phosphate.
x. Women of childbearing potential only. S=serum, U=urine. Pregnancy events will be captured starting at Day 1 following exposure to study intervention.
y. Remind females of reproductive potential of the need to avoid pregnancy while in study and adherence to the study's contraception requirements.
z. Local Pregnancy result must be available **prior to randomization** on Day 1. Local serum pregnancy test on Day 1 is allowed if it can be done, and results obtained, within 24 hours **prior to randomization.**
aa. HBV DNA testing will be performed for participants with positive anti-HBc and negative HBsAg and negative anti-HBs (past and/or current evidence). Participants must return to the clinic to provide a sample for HBV DNA testing prior to randomisation.
bb. Blood sample for HbA1c, insulin, glucose, renal, bone and inflammation biomarker assessments**: Renal:** Cystatin C, Beta-2-Microglobulin (urine), Retinol Binding Protein (RBP; urine), urine B2M/creatinine ratio, urine RPB/creatinine ratio, urine albumin/creatinine ratio, urine protein/creatinine ratio, urine phosphate, serum creatinine; **Bone:** bone specific

alkaline phosphatase, procollagen type 1-N-propeptide, type 1 collagen cross-linked C-telopeptide, osteocalcin; **Inflammation:** Interleukin-6 (IL-6), High-sensitivity C reactive protein (hs-CRP), D-dimer, Soluble CD14 (sCD14), Soluble CD163 (sCD163); insulin and glucose for HOMA-IR calculation

cc. Where local country or laboratory practices allow, whole blood (Virology) may be used for virologic analyses as described in the protocol.

dd. Where local country or laboratory practices allow, whole blood will be used for telomere length evaluation.

ee. Collect sample for these assessments ONLY if the Withdrawal visit occurs at Week 48.

ff. Where local country or laboratory practices allow, PBMC collection samples may be used for virologic analyses as described in Protocol Section 8.10.1

gg. Collect sample only if Withdrawal visit occurs at Weeks 24 or 48.

hh. At Screening, a subject number will be generated.

15.3. Appendix 3: Assessment Windows

Laboratory data, health outcomes, vital signs, e-CSSRS and genotypic and phenotypic data will be assigned to assessment windows according to actual dates rather than the nominal visit labels as recorded on the eCRF or in the laboratory database.

A window around a target Study Day will typically include all days from the midpoints between it and the target Study Days of the previous and the proceeding visits. In general, the nominal target study day for week w is (7*w)+1.

15.3.1. Definitions of Assessment Windows for Analyses

Analysis Set / Domain	Parameter (if applicable)	Target	Analysis Window		Analysis Timepoint
			Beginning Timepoint	Ending Timepoint	
Efficacy, Labs and Health outcomes (not collected at Week 52)	Laboratory Assessments (including HIV-1 RNA, lipids and biomarkers), HIVTSQ, SDM				
		-28	-4	-4	Screening
		1	-3	1	Day 1
		29	2	56	Week 4
		85	57	126	Week 12
		169	127	210	Week 24
		253	211	294	Week 36
		337	295	378	Week 48
		449	379	490	Week 64
		7*w+1	7*w-41	7*w+42	Week w, w=76, 88, ...
		Study Day of last dose + 28	>Study Day of last dose +1	>Study Day of last dose +1	Follow-up
Efficacy and Safety Data collected at Week 48 and Week 52)	Weight, BMI, eCSSRS				
		-28	-4	-4	Screening
		1	-3	1	Day 1
		29	2	56	Week 4
		85	57	126	Week 12
		169	127	210	Week 24
		253	211	294	Week 36
		337	295	350	Week 48
		365	351	406	Week 52

Analysis Set / Domain	Parameter (if applicable)	Target	Analysis Window		Analysis Timepoint
			Beginning Timepoint	Ending Timepoint	
		449	407	490	Week 64
		7*w+1	7*w-41	7*w+42	Week w, w= 76, 88, ...
		Study Day of last dose + 28	>Study Day of last dose +1	>Study Day of last dose +1	Follow-up

NOTES:

- For parameters which are not scheduled to be assessed at particular visits, the all-inclusive windows defined will still be used.
- Assessments at unscheduled visits will be included for 'any time On-treatment' time points and in data listings, as well as algorithms that make use of additional data (e.g., Snapshot).
- In the event a baseline value is missing, the latest pre-dose value prior to baseline will be used, notwithstanding this date occurring more than 3 days prior to baseline.

15.4. Appendix 4: Study Phases and Emergent Adverse Events

15.4.1. Study Phases

Data collected from both arms up to and including the date of the Week 52 visit will be considered to be during the Randomized Phase of the study.

For subjects randomized to DTG/3TC, data collected after Week 52 will be considered to be during the Continuation Phase of the study. For subjects randomized to the CAR arm, Continuation Phase of the study is not applicable.

Phase	Randomized Arm	Start	End
Randomized Phase	DTG/3TC	IP start date	Week 52 DOV -1 or Withdrawal date before Week 52 DOV -1
	CAR	Day 1 DOV	Week 52 DOV -1 or Withdrawal date before Week 52 DOV -1
Continuation Phase	DTG/3TC	Week 52 DOV	IP end date or Withdrawal date
	CAR	Not applicable	Not applicable

15.4.1.1. Study Phases for for Laboratory, HIV Associated Conditions, Vital Signs, Health Outcomes and Genotypic and Phenotypic Data

Treatment State	Definition
Pre-Treatment	Date ≤ Study Treatment Start Date
On-Treatment	Study Treatment Start Date < Date ≤ Study Treatment Stop Date + 1
Post-Treatment	Date > Study Treatment Stop Date +1

NOTES:

- If the study treatment stop date is missing then the assessment will be considered to be On-Treatment

15.4.1.2. Study Phases for Adverse Events

For adverse events, partial AE start date will use imputation as described in Section 15.7.2.1. In the case of a completely missing start date, the event will be considered to have started On-treatment unless an end date for the AE is provided which is before start of study treatment; in such a case the AE is assigned as Pre-treatment.

Treatment State	Definition
Pre-Treatment	AE Start Date < Study Treatment Start Date
On-Treatment	If AE onset date is on or after treatment start date & on or before treatment stop date. Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date
Post-Treatment	If AE onset date is after the treatment stop date. AE Start Date > Study Treatment Stop Date
Onset Time Since 1st Dose (Days)	If Treatment Start Date > AE Onset Date = AE Onset Date - Treatment Start Date If Treatment Start Date ≤ AE Onset Date = AE Onset Date - Treatment Start Date +1 Missing otherwise.
Duration (Days)	AE Resolution Date – AE Onset Date + 1
Drug-related	If relationship is marked 'YES' on eCRF.

NOTES:

- Partial AE start date will use imputation as described in Section 15.7.2.1
- In the case of a completely missing start date, the event will be considered to have started On-treatment unless an end date for the AE is provided which is before start of investigational product; in such a case the AE is assigned as Pre-treatment.
- If the IP Stop Date is missing, then any event with a start date on or after IP Start Date will be considered to be On-treatment.
- If the start date of the AE is after IP Stop Date but has been recorded as potentially related to IP, then it will be classified as On-treatment.

15.4.1.3. Study Phases for Concomitant Medication

- Prior medications: Those taken (i.e., started) before the start date of investigational product.
- Concomitant medications: Those taken (i.e., started or continued) at any time between the start date and stop date of study treatment, inclusive. Prior medications that were continued during this period are also considered as concomitant medications.
- Post treatment medications: Those started after the stop date of study treatment. Concomitant medications that were continued during this period are also considered as post-treatment medications.

It will be assumed that medication has been taken on the date in which it is reported as started or stopped. For any medication starting on the same date as study treatment, it will be assumed that the medication was taken after the subject started taking study treatment.

Duration of episodes of concomitant medication will be calculated as medication stop date – medication start date, so long as the medication is defined as concomitant according to the rules above (and presented below in the scenario matrix). Durations will be left blank if stop date is missing.

ART medications will also be classified as prior to screening, concomitant to screening and/or post-treatment according with the following modifications:

- ART starting on study treatment stop date will be considered as only post-treatment and not concomitant. It is expected that after discontinuation of study treatment, a subject may immediately begin taking another ART.
- ART stopping on study treatment start date will only be considered as prior and not concomitant.
- Any ART entered on the Prior ART eCRF with partial end date will be assumed to have finished before Screening.
- ART stopped prior to screening includes all ART that has stopped prior to screening. All ingredients from any regimen that is switched to another regimen prior to the screening visit e.g. from TDF-based to TAF-based ART will be presented as having stopped.
- ART Medications received at or after Screening includes all ART that is either being received at the screening visit or is introduced at a later date. Note, for CAR patients this could be pre- or post- randomization and for DTG/3TC patients this can be pre-randomization only; at randomization and beyond for DTG/3TC patients, ART is recorded as ‘study treatment’ and not recorded via ART-specific concomitant medication pages.
- ART Medications Received at Screening includes all ART that is ongoing at the screening visit only.

	Pre-treatment	On-treatment			Post-treatment		Prior	Concomitant	Post
(a)	x———						Y	N	N
(b)	x———-	———x					Y	Y	N
(c)	x———-	———				———x	Y	Y	Y
(d)		x———					N	Y	N
(e)		x———	IP Start Date	IP Stop Date	IP Stop Date+1	———x	N	Y	Y
(f)						x———	N	N	Y
(g)	?———x						Y	N	N
(h)	?———	———x					Y*	Y	N
(i)	?———	———				———x	Y*	Y*	Y
(j)	x———-	———				———?	Y	Y**	Y**
(k)		x———				———?	N	Y	Y**
(l)						x———?	N	N	Y
(m)	?———	———				———?	Y***	Y***	Y***
(n)	x———		x				Y	Y	N
(o)	?———		x				Y*	Y	N
(p)		———x	x				N	Y	N
(q)		———	x	x			N	Y	N
(r)				x	—	———x	N	Y	Y
(s)				x	—	———?	N	Y	Y**
(t)					x	———x	N	N	Y
(u)					x	———?	N	N	Y
(v)		x———		—	x		N	Y	Y

x = start/stop date of medication
? = missing start/stop date of medication
* If a medication is stopped On-treatment or Post-treatment and no start date is recorded it will be assumed that the medication was ongoing from the Pre-treatment phase
** If a medication is started Pre-treatment or On-treatment and no stop date is recorded then usage will be assumed to be ongoing for the remainder of the study
*** If a medication has no start or stop date it will be assumed that the medication was ongoing from the Pre-treatment phase to the Post-treatment phase

15.4.2. Combining Treatment Phases and States

On-treatment and Post-treatment assessments and events will be classified as occurring during the Randomized or Continuation Phase of the study as follow:

- If a subject did not enter the Continuation Phase, then any Post-treatment data will be assigned to the Randomized Phase.
- For subjects who did enter the Continuation Phase, any Post-treatment data will be assigned to the Continuation Phase.

For concomitant medication, if there is a duration overlapping any period then this should be reflected such that a concomitant medication (at time of the data cut):

- Starting and ending before treatment start then phase is set to missing
- Is taken at any point during the randomized phase only then phase is set to “Randomized Phase”
- Is taken at any point during the continuation phase only then phase is set to “Continuation Phase”
- Is taken at any point across the randomized and continuation phases then phase is set to “Randomized and Continuation Phase”

15.4.3. Emergent Flag for Adverse Events

Flag	Definition
Emergent	• Emergent refers to AE Severity/ Lab toxicity that develops or increases in intensity after baseline

For adverse events, partial AE start date will use imputation as described in Section 15.7.2.1. In the case of a completely missing start date, the event will be considered to have started On-treatment unless an end date for the AE is provided which is before start of investigational product; in such a case the AE is assigned as Pre-treatment.

For laboratory data, there will be no imputation of dates, which are expected to be fully complete and available in SDTM transfers. Any laboratory dates that are partially missing will be queried.

15.5. Appendix 5: Data Display Standards & Handling Conventions

15.5.1. Reporting Process

Software	
• The currently supported versions of SAS software and any other statistical reporting software required for the analysis and reporting will be used.	
Reporting Area	
HARP Server	uk1salx00175
HARP Compound	:\ARPROD\GSK3515864\mid208090*reporting_effort_number*
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1 or above). • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented as SDTM.	
Generation of RTF Files	
• RTF files will be generated for all reporting efforts.	

15.5.2. Reporting Standards

General

• The current GSK Statistical Display Standards Library will be applied for reporting, unless otherwise stated (Library Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics
• Do not include subject level listings in the main body of the GSK Clinical Study Report. All subject level listings should be located in the modular appendices as ICH or non-ICH listings
• All data displays will use the term “subjects” rather than “participants”.

Formats
• GSK Statistical Display Principles (5.03 & 6.06.3) for decimal places (DP’s) will be adopted for reporting of data based on the raw data collected, unless otherwise stated. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the GSK Standard statistical Display Principles but may be adjusted to a clinically interpretable number of DP’s.
Planned and Actual Time

• Reporting for tables, figures and formal statistical analyses:
  • Actual time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.

• Reporting for Data Listings:
  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to GSK Standard Statistical Display Principle 5.05.1).
  • Unscheduled or unplanned readings will be presented within the subject's listings.	

Unscheduled Visits	
• Unscheduled visits will be assigned to a study visit using the all-inclusive windows defined in Section 15.3. • However, data summaries will only report visits that are planned assessment time points for each parameter (according to the Time and Events table). • Assessments at unscheduled visits will be included for 'any time On-treatment' time points and in data listings, as well any algorithms that make use of additional data (e.g., Snapshot).	
Descriptive Summary Statistics	
Continuous Data	Refer to GSK Standard Statistical Display Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to GSK Statistical Display Standard Statistical Principals 7.01 to 7.13.	

15.6. Appendix 6: Derived and Transformed Data

15.6.1. General

Multiple Measurements at One Time Point

- If there are multiple assessments within Screening window, the last assessment before Day 1 will be used
- If there are multiple assessments within Day 1 window, the latest pre-dose assessment will be used
- With the exception of the Snapshot endpoints, if after window assignment (see Section 15.3), there are multiple valid assessments of a parameter within the same window, then the following hierarchy will be used to determine the value to be used for summary statistics of observed values:
    - the assessment closest to the window target Study Day;
    - if there are multiple assessments equidistant from the target Study Day, then for continuous variables the mean of these values will be used and for categorical variables the worse assessment. For HIV-1 RNA, the geometric mean of the number of copies will be used as opposed to the arithmetic mean
- Assessments not chosen for use in summary statistics by this algorithm will still appear in the associated listings. Also, such valid assessments will be used when determining values of potential clinical concern for the 'any time On-treatment' time point, and for any algorithm that has specific rules for which observation to use (e.g., SNAPSHOT).
- In the event of laboratory re-tests being performed the last re-test in the visit window will be used. For example:
- *If a subject had a week 24 viral load and then two re-tests (i.e. three viral loads labeled as week 24, unscheduled 1 unscheduled 2). and the first two viral loads were within the upper bound of the week 24 visit (Day 210) but the last re-test was slotted to week 36 then the last re-test would not be used for the week 24 snapshot.*
- *If a subject had a week 24 viral load but the re-test was performed on Day 220 (week 36) then the re-test viral load would not be used for the week 24 snapshot.*

Study Day

- Calculated as the number of days from initial study treatment start date:
    - Ref Date = Missing → Study Day = Missing
    - Ref Date < Treatment Start Date → Study Day = Ref Date –Treatment Start Date
    - Ref Data ≥ Treatment Start Date → Study Day = Ref Date – (Treatment Start Date) + 1

Note that Treatment Start Date is considered to be on Study Day 1 and the day before this is Study Day -1; i.e., there is no Study Day 0.

Post-baseline

- Post-baseline refers to the combined time periods of On-treatment and Post-treatment. Post-baseline may be further specified according to phase of the study: Randomized Phase and Continuation Phase.

Study Drug

- Study Drug refers to either Investigational Product DTG/3TC or CAR.

15.6.2. Study Population

Demographics

Age

- Age, in whole years, will be calculated with respect to the subject's Screening visit where year of birth is collected.
- GSK Statistical Display Standard algorithms will be used for calculating age where birth date will be imputed as follows:
  - For all subjects, the missing date and month will have this imputed as '30th June'.
  - For analysis purposes, if a subject did not fail to meet inclusion criteria #1 (aged 18 years or older), then set any age imputed as <18 by the GSK Statistical Display Standard algorithm to 18. If the subject failed to meet inclusion criteria #1 then the imputed age will not be reset.
- Birth date will be presented in listings as 'YYYY'.
- Completely missing dates of birth will remain as missing, with no imputation applied. Consequently, the age of the subject will not be calculated and will remain missing.

Framingham Risk Equation

The predicted probability, $\hat{p}$, of having a cardiovascular disease (CVD) within the next 10-years according to the Framingham formula [D'Agostino 2008] is

for females:

$$\hat{p}_F = 1 - S_0(t)^{\exp\{2.32888 \times \log(\text{age}) + 1.20904 \times \log(TC) - 0.70833 \times \log(HDL) + 2.76157 \times \log(SBPu) + 2.82263 \times \log(SBPt) + 0.52873 \times I_s + 0.69154 \times I_d - 26.1931\}},$$

for males:

$$\hat{p}_M = 1 - S_0(t)^{\exp\{3.06117 \times \log(\text{age}) + 1.12370 \times \log(TC) - 0.93263 \times \log(HDL) + 1.93303 \times \log(SBPu) + 1.99881 \times \log(SBPt) + 0.65451 \times I_s + 0.57367 \times I_d - 23.9802\}},$$

where

$$S_0(t) = \begin{cases} 0.95012, \text{females} \\ 0.88936, \text{males} \end{cases}$$

TC = total serum cholesterol (mg/dL),

HDL = serum HDL cholesterol (mg/dL),

$SBPu$ = systolic blood pressure (mmHg) if subject is not treated for high blood pressure (note that if a subject is treated for high blood pressure then log($SBPu$) = 0)

$SBPt$ = systolic blood pressure (mmHg) if subject is treated for high blood pressure (note that if a subject is not treated for high blood pressure then log($SBPt$) = 0)

$$I_s = \begin{cases} 1, \textit{current smoker} \\ 0, \textit{otherwise} \end{cases}$$

$$I_d = \begin{cases} 1, \textit{diabetic} \\ 0, \textit{otherwise} \end{cases}$$

Demographics
• A subject will be considered as treated for high blood pressure if at Screening/Day 1 visit the subject receives any medication for hypertension (need to check whether any of the terms "HYPERTENSION", "HYPERTENTION", "HIPERTENSION" or similar is included in the description of SDTM.CM.CMINDC variable) • Smoking status is collected on Screening/Day 1 visit as "Never smoked", "Current smoker", "Former smoker". For "Current smoker" I_s should be set to 1 and for "Never smoked" and "Former Smoker" I_s should be set to 0. • A subject is classified as diabetic if "Current" or "Past" has been selected in the medical history eCRF page completed on Screening/Day 1 visit; if "Not assessed" has been selected then the subject will be considered diabetic if the subject receives any medication for diabetes on Screening/Day 1 visit (need to check whether any of the terms "DIABETES" or "DIABETIC" is included in the description of SDTM.CM.CMINDC variable). • The 10-year probability of CVD will not be calculated for subjects who have indicated "Current "or "Past" myocardial infarction in the medical history eCRF page completed on Screening/Day 1 visit. These subjects will not be included in summary statistics (e.g. mean, sd, median) of 10-year CVD risk in 'Summary of Baseline Cardiovascular Risk Assessments Table',but will be counted in the highest category of risk (i.e. >20%) in the summary by category.
Extent of Exposure
• Exposure to DTG/3TC will be calculated from the IP eCRF pages. Exposure to CAR will be calculated from the CONART eCRF pages. • Subjects who were randomized to DTG/3TC but did not report a IP start date will be categorised as having zero days of exposure. • Subjects who were randomized to CAR but withdrew on Day1 will be categorised as having zero days of exposure • Missing Treatment Stop Date will be imputed, for purposes of calculating exposure, as the date of last visit or the recorded date of withdrawal/completion, whichever is earlier. • Actual exposure will be calculated where the duration of any dosing interruptions based on eCRF data will be subtracted from the result above. • The ratio (percentage) of the actual exposure to the overall exposure (i.e. study treatment stop date – study treatment start date+1) will be used to define protocol deviation leading to exclusion from PP Population due to study treatment interruption (i.e. >10%).
Strata
• For analysis purposes, randomization strata will be used from that derived using eCRF data, even if this differs from the strata captured in IVRS. • For patients randomized to DTG/3TC, baseline third agent class is collected on the prior ART history form. For patients randomized to current CAR, baseline third agent class is collected on the concomitant ART form. • Third agent class is identified using terms from the GSK Drug Dictionary

15.6.3. Efficacy

HIV-1 RNA

Snapshot

- It is intended to be primarily a virologic assessment of the endpoint, and as such follows a "virology first" hierarchy.
- Plasma HIV1-RNA < 50 c/mL or plasma HIV1-RNA ≥ 50 c/mL within an analysis window is typically determined by the last available plasma HIV-1 RNA measurement in that window while the subject is On-treatment.
- When no HIV-1 RNA data is available within a window, a subject cannot be classified under HIV1-RNA < 50 c/mL. Depending on the reason for lack of data, the subject will be classified as a HIV1-RNA ≥ 50 c/mL or reported as 'No Virologic Data at Week X'; in the latter case, the algorithm further classifies the nature of the missing data. Typically, a subject withdrawn (i) due to AE or, (ii) for another reason yet was suppressed at the time, will be counted as 'No Virologic Data at Week X'. Should a subject withdraw for reasons other than AE and was not suppressed at the time, they will be a HIV1-RNA ≥ 50 c/mL.
- For each scheduled assessment time, the snapshot response rate for a given threshold (e.g., <50 c/mL) is defined as:

$$\text{Snapshot Rate} = \frac{\text{Number of responders in that analysis window}}{\text{Number of subjects in the analysis population}}$$

- Full details of the algorithm, including the handling of special cases, are included in Section 15.11 of note, the date at which the subject 'discontinue/withdrawn from the study' in the Snapshot algorithm is the date of treatment discontinuation, rather than the date of study withdrawal,

Plasma HIV-1 RNA

- For summaries and analyses which use HIV-1 RNA level as a continuous measure, the logarithm to base 10 of the value will be used.
- HIV-1 RNA results may be provided as censored values, such as <40 or >9,999,999 c/mL. For the purposes of summary statistics, such values will be replaced by the next value beyond the limit of detection, e.g., 39 or 10,000,000 c/mL, respectively, for the given examples. Data listings will show the censored values as provided.
- Qualitive measures (i.e. "target detected" and "target non-detected") may also be provided by the laboratory vendor for values <40 c/ml. When a measurement of plasma HIV-1 RNA is below the limit of quantification (i.e. 40 c/mL) and is qualitatively observable that will be denoted as a "Target Detected" measure, while HIV-1 RNA below the limit of quantification that is not qualitatively observable that will be denoted as "Target Not Detected". Any measurements <40 c/mL characterised as "Target Non-Detected" or "Target Detected" will be captured in the database.

Confirmed Virologic Withdrawal (CVW), Suspected Virologic Withdrawal (SVW) and Precautionary Virologic Withdrawal (PVW) and potential Precautionary Virologic Withdrawal (pPVW)

Please refer to the protocol, Section 7.1.1 for more details of the derivation of CVW, PVW, pPVW and SVWs.

HIV-1 RNA

PVW (leading to discontinuation)

- May be met after two consecutive assessments with HIV-1 RNA >=50 and <200 c/mL without an identifiable, non-virologic cause (immunization, illness, nonadherence) and after discussion with Medical Monitor, OR
- Will be met with three consecutive on treatment assessments with HIV-1 RNA >=50 and <200 c/mL

pPVW

- Will be met after two consecutive assessments with HIV-1 RNA >=50 and <200 c/mL. The current HIV-1 RNA values **must** be below 200 c/mL, but the previous HIV-1 RNA can also have been >=200 c/mL

SVW

- One assessment with HIV-1 RNA >= 200 c/mL after Day 1 with an immediately prior HIV-1 RNA <50 c/mL.

CVW

- One assessment with HIV-1 RNA >= 200 c/mL after Day 1 with an immediately prior HIV-1 RNA >=50 c/mL

General Considerations

- The subsequent HIV-1 RNA sample taken after SVW will be used for the determination of CVW.
- Based on the protocol specific conditions outlined in the protocol, derivation of SVW and CVW will use nominal visits and unscheduled visits.
- Visit windowing will not be applied.
- The condition of 2-4 weeks between the suspected and confirmatory re-test (as described in protocol Section 7.1) will not be used when programmatically identifying CVW.
- A patient can only be classified as CVW for the analyses if the patient has not withdrawn IP at the time of the HIV-RNA re-test value (at CVW value), where Treatment Start < HIV-1 RNA sample date <= Treatment Stop Date + 1 (if Treatment Stop date exists). Note: study drug interruptions will not be taken into account when programmatically identifying CVW.
- Similarly, viral loads above criteria cut-offs resulting in SVW, CVW, PVW and pPVW need to have occurred post-Day 1 in order for the criteria to be met. For example an SVW can occur at Week 4 if Week 4 HIV-1 RNA >=200 i.e. the viral load above SVW criterion occurred post-Day 1.
- Additional guidelines specified in the protocol related to patient management only and will not be taken into account when programmatically identifying CVW.
- The SVW can become a pPVW, and then later a PVW, if the confirmatory viral loads are between 50 and 200 c/mL
- Please refer to Section 7.1.1 of the protocol for details of the derivation.

CDC HIV-1 Classification and HIV-associated conditions

- HIV associated conditions will be assessed according to the 2014 CDC Revised Classification System for HIV Infection in Adults (see protocol Section 11.12).

HIV-1 RNA
• Any 'other' conditions reported in the eCRFs will be identified programmatically before being sent for clinical review to determine whether they should be classed as stage 3 associated conditions. Review will be ongoing and as a minimum will take place prior to each reporting effort.

15.6.4. Safety

Extent of Exposure
• Exposure to DTG/3TC will be calculated from the IP eCRF pages. Exposure to CAR will be calculated from the CONART eCRF pages. Number of days of exposure to study drug will be calculated as: Duration of Exposure in Days = (Treatment Stop Date –Treatment Start Date) + 1 For subjects randomized to DTG/3TC or CAR at Day 1: • For Randomized Phase: o For patients completing the Randomized Phase Exposure = IP Start Date to (Week 52 DOV -1) o If a subject discontinues prior to Week 52, the IP Stop Date recorded in the eCRF will be used. A partial or missing IP stop date is handled as described in Section 15.7.2.1. o A Day 1 Date of Visit will be used for partial or missing IP start date. • The overall exposure is calculated as o Exposure = IP Stop Date – IP Start Date + 1 • Duration of dosing in subject years will be calculated as the sum of subject duration of dosing in days (across all subjects)/365.25 • Subjects who were randomized to DTG/3TC but did not report a IP start date will be categorised as having zero days of exposure. • Subjects who were randomized to CAR but withdrew on Day1 will be categorised as having zero days of exposure. • Missing Treatment Stop Date will be imputed, for purposes of calculating exposure, as the date of last visit or the recorded date of withdrawal/completion, whichever is earlier. • An alternative calculation of exposure will be performed where the duration of any dosing interruptions based on eCRF data will be subtracted from the result above. • The ratio (percentage) of the actual exposure to the overall exposure (i.e. study treatment stop date – study treatment start date+1) will be used to define protocol deviation leading to exclusion from PP Population due to study treatment interruption (i.e. >10%).
Adverse Events
AE Severity – DAIDS Grading
• The DAIDS grading (VERSION 2.1, March 2017) for severity of clinical adverse events will be performed.

Extent of Exposure

- See protocol for DAIDS grading criteria.

Adverse Events of Special Interest (AESI)

The preferred terms for each AESI will be review by safety and clinical team and updated before each formal analysis in a separate document. The following table below shows the AESI categories.

AESI
Anxiety
Depression and hypomania
Drug Hypersensitivity
Insomnia
Nightmare/Abnormal Dreams
Rash
Sleep disorder
Suicidality and self-injury

Laboratory Parameters

- Additional non-protocol specified laboratory assessments performed at the institution's local laboratory that are databased will not be included in the listings or analyses/summaries. All analyses will be based on central laboratory assessments only. If a laboratory value which is expected to have a numeric value for summary purposes, has a non-detectable level reported in the database, where the numeric value is missing, but typically a character value starting with '<x' or '>x' (or indicated as less than x or greater than x in the comment field) is present, the number of significant digits in the observed values will be used to determine how much to add or subtract in order to impute the corresponding numeric value.
  - Example 1: 2 Significant Digits = '< x ' becomes x – 0.01
  - Example 2: 1 Significant Digit = '> x' becomes x + 0.1
  - Example 3: 0 Significant Digits = '< x' becomes x – 1

Lab Toxicities – DAIDS Grading

- Toxicities will be based on the Division of AIDS (DAIDS) grading system, as specified in the protocol.
- Toxicity grades provided by the central laboratory do not distinguish between abnormally high or low criteria, when both are relevant for a particular parameter.
- When summarising toxicity grades for such parameters, they will be categorised as to whether they are above or below the midpoint of normal range.

Parameter	Below Midpoint	Above Midpoint
Calcium	Hypocalcaemia	Hypercalcaemia
Fasted glucose	Hypoglycaemia	Hyperglycaemia
Sodium	Hyponatremia	Hypernatremia
Potassium	Hypokalemia	Hyperkalemia

Lipid-Modifying Agents

- The following ATC codes correspond to lipid-modifying agents:
  - ATC Level 2: C10
  - ATC Level 3: C10A, C10B (if Level 2 is not available)

Laboratory Parameters

- ATC Level 4: C10AA, C10AB, C10AC, C10AD, C10AX, C10BA, C10BX (if level 2, 3 are not available)

- Subjects are considered to have used a lipid modifying agent at baseline if they were taking the medication at the time of their baseline laboratory assessment or if they stopped their lipid modifying medication within 12 weeks of their baseline lipid testing date.

National Cholesterol Education Program (NCEP) Lipids Categories

- In addition to DAIDS toxicity scales (see protocol), lipid values will be categorized according to the 2001 NCEP Adult Lipid Guidelines [Grundy, 2001].

Parameter	Value Range (mmol/L)	Value Range (mg/dL)	Category
Triglycerides	<1.70	<150	Normal
	1.70 to <2.26	150 to <200	Borderline High
	2.26 to <5.65	200 to <500	High
	≥5.65	≥500	Very High
Total Cholesterol	<5.18	<200	Desirable
	5.18 to <6.21	200 to <240	Borderline High
	≥6.21	≥240	High
HDL Cholesterol	<1.04	<40	Low
	1.04 to <1.56	40 to <60	Normal
	≥1.56	≥60	High
LDL Cholesterol	<2.59	<100	Optimal
	2.59 to <3.37	100 to <130	Near/Above Optimal
	3.37 to <4.14	130 to <160	Borderline High
	4.14 to <4.92	160 to <190	High
	≥4.92	≥190	Very High

Total Cholesterol / HDL Cholesterol Ratio

- When both total cholesterol and HDL cholesterol results are available from the same date for a subject, then the ratio will be calculated by dividing the total cholesterol result by the HDL cholesterol result. The ratio can be classified as follows:

Parameter	Value Range
Total Cholesterol / HDL Ratio	< 3.5
	3.5 to < 4.4
	4.4 to < 5
	≥ 5

Glomerular Filtration Rate (GFR)

- Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [Levey et al.] will be used by the central laboratory to provide an estimate of GFR, in mL/min per 1.73 m2, as follows for the CKD-EPI creatinine equation:

$$GFR = 141 \times \min\left(\frac{CRT_{mg/dL}}{\kappa}, 1\right)^{\alpha} \times \max\left(\frac{CRT_{mg/dL}}{\kappa}, 1\right)^{-1.209} \times 0.993^{Age} \times [1.018 \text{ if Female}] \times [1.159 \text{ if Black}]$$

Laboratory Parameters

where age (in years) is at time of assessment, κ = 0.7 if female or 0.9 if male, α = -0.329 if female and -0.411 if male, min() indicates the minimum of CRT/κ or 1, max() indicates the maximum of CRT/κ or 1, and CRTmg/dL is serum creatinine concentration in mg/dL. The serum creatinine concentration in mg/dL is obtained from GSK standard units of μmol/L as CRTmg/dL =0.0113x CRTμmol/L.

CKD-EPI Cystatin C Equation (2012)

The following will be used for the CKD-EPI Cystatin C Equation:

$eGFR = 133 \times \min(Scys/0.8, 1)^{-0.499} \times \max(Scys/0.8, 1)^{-1.328} \times 0.996^{Age} \times 0.932$ [if female]

Abbreviations / Units

eGFR (estimated glomerular filtration rate) = mL/min/1.73 m2

Scys (standardized serum cystatin C) = mg/l

min = indicates the minimum of Scys/0.8 or 1

max = indicates the maximum of Scys/0.8 or 1

age = years

Assays

Hepatitis Status

- Hepatitis C status will be determined using antibody (IgM or IgG) and/or hepatitis C virus (HCV) RNA assessments performed during screening.
- If both antibody and virus RNA assessments are available, then the latter will take precedence and positive/negative status will be based on whether HCV RNA is detectable (i.e., ≥43 IU/mL [≥1.63 log IU/mL]) or not
- Antibody (IgM or IgG) status with 'BORDERLINE' or 'REACTIVE' will be considered Positive
- A subject will be considered positive for hepatitis B virus (HBV) if they have a positive surface antigen or detectable HBV DNA result during screening. Subjects positive for HBV are not allowed to enter the study.

BMI

- BMI classification is based on standard categories adopted by the WHO and FDA:
  Underweight = BMI of < 18.5 kg/m2
  Normal = BMI of 18.5 – 24.99 kg/m2
  Overweight = BMI of 25 – 29.99 kg/m2
  Obese = BMI of ≥ 30 kg/m2

Other Safety Endpoints

Columbia Suicide Severity Rating Scale (C-SSRS)

- Missing data will not have any imputation performed.
- A positive alert is triggered if a subject has reported suicidal ideation/behaviour in categories 4-9.
- Questions in categories 3-5 will be triggered if suicidal ideation is reported in categories 1 or/and 2.
- Incomplete calls:
    - when no complete call is databased on the same day, the data from the incomplete call will be used
    - if a subject has only an incomplete call, and it resulted in a positive alert, the relevant pages in the eCRF should be completed, even though the call was incomplete
    - when a complete call is databased on the same day, the data from the complete call will be used in the summaries.
- Duplicate calls, if they occur on the same day:
    - Both calls will be reported in the listings.
    - For summary tables, the entry with latest time record will be used.
    - For summary tables at baseline, unscheduled repeat visits will not be summarised.
    - Relevant eCRF pages will be completed based on the latest entry (if it was a positive alert).
- Late Day 1 assessments
    - Late DAY 1 assessments will be summarised as representing baseline status (i.e., treated as true DAY 1 assessments). Where this leads to multiple DAY 1 assessments, 'complete' assessments will be used over 'incomplete' assessments to represent baseline status. Such assessments will be considered DAY 1 if they occur by Day 14.
- Day 1 assessments performed at later visits
    - DAY 1 assessments on (or close to) study day 1 will be accepted as DAY 1 assessments (as above). For DAY 1 assessments performed at later visits, the 'Lifetime' assessment observation will not be summarised but the 'Within the past 2 months' assessment will be used as a surrogate for the later post-baseline visit assessment.

Homeostatic model assessment-Insulin Resistance (HOMA-IR)

- HOMA-IR = (fasting plasma insulin (mU/L) * fasting plasma glucose (mmol/L)) / 22.5.
- HOMA-IR categories will be categorised as follows:
  - <2
  - 2 to <3
  - 3 to <4
  - >=4

  All HOMA-IR analyses will be based on fasting values and only patients with post-baseline values will be included in analyses (i.e. patients with missing post-baseline HOMA-IR will not be included in summary tables or figures). Additionally, patients who are diabetic as captured on the medical history form at screening will be excluded from all HOMA-IR analyses. Finally, any patient who has taken an anti-diabetic medication (ATC code "A10" (**DRUGS USED IN DIABETES)**) as captured on the medical history form up to screening will be removed from the analysis.

15.6.5. Viral Genotyping and Phenotyping

Genotype

Amino Acid Changes

- A mutation is considered present whenever the encoded amino acid residue differs from the amino acid that would have been encoded by the wild-type (e.g., HXB2, NL43) comparator gene; e.g., Q148K.
- If the encoded amino acid is seen as a mixture of wild-type and mutant amino acid, e.g., Q148Q/K, the mutated amino acid is considered present at the codon of interest.
- If the encoded amino acid is seen as a mixture of two or more amino acids, which may or may not include wild type, e.g., Q184K/H or Q184K/H/Q, etc., for the purposes of calculating the number of mutated amino acids, only one mutation is considered to be present at the codon of interest.

Representation of Amino Acid Changes

Mutations	Amino acid change
T69S	Single mutation from amino acid 'T' (vendor reference) to 'S' (sample) at codon '69'
Q148H/K/R	Mixture of amino acid mutations 'H', 'K' and 'R' (sample) from amino acid 'Q' (vendor reference) at codon '148'
_69_1T	First insertion of amino acid 'T' (sample) at codon '69'
_69_2S	Second insertion of amino acid 'S' (sample) at codon '69'
_69_3S/A	Third insertion of a mixture of amino acids 'S' and 'A' (sample) at codon '69'
L74L/-	Mixture of amino acid 'L' (sample) and a deletion at codon '74'
V75-	Single deletion of amino acid (sample) at codon '75'

Resistance Associated Mutations

- Known INI mutations associated with the development of resistance to RAL, EVG, BIC or DTG:

Amino Acids in HIV Integrase for Analysis	H51Y, **T66A/I/K**, L74M, **E92Q/V**/G, Q95K, T97A, G118R, **F121Y**, E138A/K/D, G140A/C/S, **Y143C/H/R/K/S/G/A, P145S**, **Q146P**, **S147G**, **Q148H/K/R**, **V151**I/**L**/A, S153F/Y, **N155H/**S/T, E157Q, G163R/K, S230R, R263K, L68V/I*, L74I*, E138T*, V151I*, G193E*

NOTES:

- Current listing includes INSTI mutations identified via the Stanford HIV Resistance database, or identified during in vitro passage of DTG*, or as seen in a previous DTG studies in INI-experienced subjects* (i.e. ING112574) and may be modified in case of additional substantive data availability. This table is updated only by Virologists.
- INI mutations listed taken from Stanford HIV Resistance Database (http://hivdb.stanford.edu/DR/cgi-bin/rules_scores_hivdb.cgi?class=INI cited 25 Oct 2019) and accessed on 28 Oct 2020.
- Each INI mutation listed had a score of ≥15. INI substitutions listed above in bold had a score for EVG or RAL of =60.

- Major resistance mutations to other classes (i.e., NRTI, NNRTI, PI) as defined by the International Antiviral Society-USA (IAS-USA). The most up to date IAS-USA guidelines available at the time of DBF will be used in the analysis.

Genotype

Amino Acid Changes

Class	Mutations
NRTIs	M41L, A62V, K65R/E/N, D67N, 69 insert, K70E/R, L74V, V75I, F77L, Y115F, F116Y, Q151M, M184V/I, L210W, T215Y/F, K219Q/E
NNRTIs	L100I, K101E/P, K103N/S, V106A/M, V108I, E138/A/G/K/Q/R, V179L, Y181C/I/V, Y188C/L/H, G190S/A, H221Y, P225H, F227C, M230I/L,
PIs	D30N, V32I , M46I/L, I47A/V, G48V, I50V/L, I54M/L/V, Q58E, T74P, L76V, V82A/T/F/L/S, N83D, I84V, N88S, L90M

Note: List generated from IAS_USA Guideline, - 2019 Drug Resistance Mutations Update Volume 27, Issue 3, September /October 2019

Susceptibility Scores

Stanford Genotypic Susceptibility Score (S-GSS)

- To establish genotypic susceptibility to ART treatment, a genotypic sensitivity score will be calculated.
- Genotypic sensitivity to each drug will be assessed using the HIVdb, the Integrated Genotypic Resistance Interpretation System [Liu, 2006].
- In the Stanford HIVdb system, each HIV-1 drug resistance mutation is assigned a drug penalty score. Also, for combination of specific mutations an extra penalty is assigned. The penalty scores for each drug resistance mutation and for combination of drug resistance mutations at different positions within each genomic region are available here

  NNRTI: https://hivdb.stanford.edu/dr-summary/mut-scores/NNRTI/
  NRTI: https://hivdb.stanford.edu/dr-summary/mut-scores/NRTI/
  PI: https://hivdb.stanford.edu/dr-summary/mut-scores/PI/
  INSTI: https://hivdb.stanford.edu/dr-summary/mut-scores/INSTI/.

- Any mutations that are not included the Stanford database will contribute 0 to the GSS calculations.
- The drug resistance estimate is obtained by adding together the penalty scores from all mutations associated with resistance to that drug and by adding also the penalty for combinations of certain mutations, if present, and then a numeric score (S-GSS) is applied for each drug as shown in the Table below.
- When there's a mixture of two or more mutations at the same position, the mutation associated with the largest penalty is scored.
- The HIVdb S-GSS will be calculated for all subjects with genotypic data at all time points from when genotypic data are available for all drugs in the Stanford database. However, Tables will report S-GSS scores only for drugs that have been taken by at least one subject during the study. Listings will report S-GSS scores for all drugs in the Stanford database.

- Examples

Example 1: Assume a subject at a specific time point has the INSTI mutations G140S and Q148H. The following Table shows the calculation of drug resistance estimate score for drugs DTG and EVG.

Penalty Scores

Genotype

Amino Acid Changes

INSTI mutations	DTG	EVG
G140S	10	30
Q148H	25	60
G140S + Q148H	10	0
Total (drug resistance estimate)	45	90

For DTG, mutation G140S has a penalty score of 10, mutation Q148H has a penalty score of 25. One need also to account for the penalty score for the combination of the two mutations which is 10. The sum of all penalties scores gives the drug resistance estimate score which is 45 in this case. Similar calculation for EVG applies.

Example 2: Assume a subject at a specific time point has the INSTI mutations: G140A/C/S (i.e. recorded as G140A, G140C and G140S in SDTM.PF) and Q148H/K/R. The following Table shows the calculation of drug resistance estimate score for DTG.

	DTG	
INSTI mutations	Individual Mutation Penalty Score	Penalty scores used for drug resistance calculation
G140A	10	
G140C	10	10
G140S	10	
Q148H	25	
Q148K	30	30
Q148R	25	
G140A/C/S + Q148H/K/R	10	10
Total (drug resistance estimate)		50

For mixture of mutations at the same position, the mutation associated with the largest penalty is used, hence for Q148H/K/R the penalty score of 30 for Q148K is used. For G140A/C/S all mutations have the same score 10 so, 10 is used. The penalty score for the combination of mutations at codon positions 140 and 148 is 10. The sum of the three penalties scores gives the drug resistance estimate score which is 50.

- Scores for particular patterns of INSTI, NNRTI, NRTI and PI mutations have been calculated and are readily available here
  NNRTI: https://hivdb.stanford.edu/dr-summary/pattern-scores/NNRTI/
  NRTI: https://hivdb.stanford.edu/dr-summary/pattern-scores/NRTI/
  PI: https://hivdb.stanford.edu/dr-summary/pattern-scores/PI/
  INSTI: https://hivdb.stanford.edu/dr-summary/pattern-scores/INSTI/

- The drug resistance estimate is obtained by adding together the penalty scores from all mutations associated with resistance to that drug and then a numeric score (S-GSS) is applied for each drug as shown below. Any mutations that are not included the Stanford database will contribute 0 to the GSS calculations. When there's a mixture of two or more mutations at the same position, the mutation associated with the largest penalty is scored. The sum scores are

Genotype

Amino Acid Changes

titrated to fall within the following ranges: susceptible, potential low-level resistance, low-level resistance, intermediate resistance, and high-level resistance (see table below).

•

Resistance Estimate	S-GSS Score	Sensitivity
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.		

- The HIVdb GSS will then be calculated for each subject defined as the sum of the resistance scores for each of their background drugs.

Monogram Genotypic Susceptibility Score (M-GSS)

- Genotypic sensitivity to each drug will be assigned using the Monogram resistance score and will be reported in a listing for all drugs where Monogram resistance score is available in the database.
- Assays PSGT, GSIN, PSGTIN denote Genotypic Sensitivity as 'Sensitive' or 'Resistance' whereas assay GSARC as 'Sensitive', 'Resistance Possible' or 'Resistance'.
- Genotypic Sensitivity provided by Monogram based on assays PSGT, GSIN, PSGTIN is translated to a Genotypic Sensitivity Score (M-GSS) according to the table below.
- For the DTG/3TC arm a subject might have a M-GSS score of 0, 1 or 2, and in the CAR arm a subject might have a M-GSS score of 0, 1, 2, or 3 (since CAR is a 3-drug regimen).

Score	Sensitivity
CCI	

Phenotype

Phenotypic Susceptibility Scores (PSS)

- Phenotypic susceptibility to all licensed antiretroviral drugs and DTG will be determined using PhenoSense HIV assays from Monogram Inc. and will be reported as fold change (FC) in IC50 relative to wild-type control virus NL4-3, i.e., FC of sample virus = IC50 of sample virus/IC50 of control virus.
- Since the maximum assay limit for FC for each ART varies from subject to subject, FC values that are greater than the maximum assay limit (e.g., '>100') will be interpreted as having a value equal to the smallest maximum assay limit for that ART in the study population for data analysis. Censored values will be presented 'as is' in the listings.

- Phenotypic susceptibilities will be categorised according to FC (based on Monogram PhenoSense assay). Clinical cut-offs (where available) or biological cut-offs by PhenoSense will be used to define the phenotypic susceptibility of background treatment.
- Replication capacity is generated as part of standard phenotypic assays.

- To establish susceptibility to background treatment, a phenotypic sensitivity score will be calculated. Phenotypic susceptibility to each drug in a subject's background regimen will be determined by applying drug-associated cutoffs as defined by the PhenoSense algorithm to the phenotypic fold resistance to that drug at a certain timepoint (e.g., Screening or Baseline). A numeric score will be assigned to each background drug using two different methods: one with full sensitivity only (PSSf) and one with partial sensitivity included (PSSp).

PSS with Full Sensitivity Only (PSSf)

Fold Change	Score	Interpretation
> clinical lower cutoff or biologic cutoff	CCI	
≤ clinical lower cutoff or biologic cutoff		

PSS with Partial Sensitivity Included (PSSp)

Fold Change	Score	Interpretation
> clinical higher cutoff	CCI	
≤ clinical higher cutoff and > clinical lower cutoff		
≤ clinical lower cutoff		

- Both PSSf and PSSp will be calculated separately for each subject defined as the sum of the resistance scores for each background drug.

Drug	Abbreviation	Class	PhenoSense cutoff
Abacavir	ABC	NRTI	(4.5 – 6.5)[a]
Lamivudine	3TC	NRTI	3.5[a]
Didanosine	ddI	NRTI	(1.3 – 2.2)[a]
Stavudine	d4T	NRTI	1.7[a]
Zidovudine	AZT (ZDV)	NRTI	1.9
Emtricitabine	FTC	NRTI	3.5
Tenofovir	TDF	NRTI	(1.4 – 4)[a]
Delavirdine	DLV	NNRTI	6.2
Efavirenz	EFV	NNRTI	3
Nevirapine	NVP	NNRTI	4.5
Etravirine	ETR	NNRTI	(2.9-10)[a]
Rilpivirine	RPV	NNRTI	2.0
Fosamprenavir/r	FPV/r	PI	(4-11)[a]
Atazanavir/r	ATV/r	PI	5.2[a]
Indinavir/r	IDV/r	PI	10[a]
Lopinavir/r	LPV/r	PI	(9 – 55)[a]
Nelfinavir	NFV	PI	3.6
Saquinavir/r	SQV/r	PI	(2.3 – 12)[a]
Tipranavir/r	TPV/r	PI	(2 – 8)[a]
Darunavir/r	DRV/r	PI	(10 – 90)[a]

Ritonavir	RTV	PI	2.5
Enfuvirtide	T20	FI	6.48
Raltegravir	RAL	INI	1.5
Elvitegravir	EVG	INI	2.5
Dolutegravir	DTG	INI	(4-13) [a]
Bictegravir	BIC	INI	(2.5-10)

a. clinical cutoff (lower cutoff – higher cutoff)

Phenotypic Susceptibility Score (PSS)

Net Assessment and Overall susceptibility of ARTs

- Net assessment is an assessment of antiviral activity of ARTs using both genotypic and phenotypic test results interpreted through a proprietary algorithm (from Monogram Biosciences) and provides the overall susceptibility of the drug (Note: partially sensitive and resistant calls are considered resistant in this analysis).
- For determining overall susceptibility of ARTs (OSS), a binary scoring system (0= CCI [redacted] 1= CCI [redacted] for each antiretroviral agent was used and will be provided in the Monogram dataset. OSS will be calculated as the sum of the net assessment scores of ARTs comprising the subject's ART and categorised as 0, 1, 2, or 3. OSS values will be calculated only for the time of CVW when net assessment is available.

Decision tree approach for Monogram resistance data analyses

- We might have resistance data that come from mixed datasets: PSGT, PSIN, GSIN (primary assays) vs PSGT+IN (secondary assay)
- If one of the primary assay does not work for a specific timepoint, we might report the secondary assay if data is available. If all primary assays for a specific timepoint work then we report primary. For example, for baseline if the same assay section (PSGT, PSIN, GSIN) worked then we report primary. If at least one of PSGT or PSIN or GSIN didn't work then we report secondary PSGT+IN.
- Secondary assay testing results might not always be available.

Background :

- PSGT - provides both geno and pheno data for PRO/RT (NRTI and NNRTI) only, with pheno including PRO/RT Replication Capacity (RC)
- PSIN - Provides pheno data on Integrase only, with pheno including IN RC
- GSIN - Provides geno data on Integrase only, This assay provides NO RC data.
- PSGT+IN - Secondary assay used if PSGT or GSIN assay fails; it provides both geno and pheno data on PRO, RT and Integrase

- If one of the primary assays does not work for a specific timepoint, we might report the data from the secondary assay, if available. If all primary assays for a specific timepoint work, then we use the data from the primary assays, as secondary assay analysis is not performed. If at least one of PSGT or PSIN or GSIN haven't worked for a specific time point (e.g. Baseline, CVF or time of switch from DTG + 3TC FDC), then we use data from the secondary PSGT+IN and the data from any primary assay that worked from this time point are ignored.
- Secondary assay testing results might not always be available.
- The decision tree algorithm will be used for data summaries in Tables. Listings will report all data from all assays that worked at a specific time point.
- For examples please refer to decision tree below.

Table Symbol Key:

Y = assay test successful
N = assay test failure
2nd = back up test performed
bold = assay to use for analysis

How to make decisions:

Scenario 1: if primary PSGT, PSIN and GSIN assays all work for both Baseline and CVF or at time to switch due to Baseline resistance mutations samples, then PSGT+IN assay will not be performed and no PSGT+IN data should be generated.

Assays	Baseline	CVF or Switch
PSGT	**Y**	**Y**
PSIN	**Y**	**Y**
GSIN	**Y**	**Y**

Scenario 2: If PSGT, PSIN and GSIN all work for Baseline sample; PSGT works for CVF or at time of Switch sample but PSIN and GSIN fail, while PSGT+IN works, then use PSGT+IN (PR, RT and INSTI) for CVF/Switch and a PSGT, PSIN, GSIN for Baseline; do not use PSGT data at CVF/Switch.

Assays	Baseline	CVF or Switch
PSGT	**Y**	Y
PSIN	**Y**	N
GSIN	**Y**	N
2nd PSGT+IN	-	**Y**

Scenario 3: If PSGT works for Baseline, but PSIN and GSIN fail, then secondary PSGT+IN assay will be performed on Baseline sample. Similarly, if PSGT works for CVF or switch sample but PSIN and GSIN fail to work, in this scenario, use data generated from PSGT+IN assay on both Baseline and CVF/switch sample for analyses, regardless of obtained PSGT assay data. Same is the case if PSGT fails in both time points and PSIN and GSIN do not fail; the data from PSGT+IN from both time points will be used.

Assays	Baseline	CVF or Switch
PSGT	Y	Y
PSIN	N	N
GSIN	N	N
2nd PSGT+IN	**Y**	**Y**

Scenario 4: If PSGT works but GSIN and PSIN both fail on Baseline sample, then 2nd PSGT+IN assay might be performed. If PSGT, PSIN and GSIN all work for CVF or Switch sample, then use Baseline PSGT+IN data from Baseline, regardless of PSGT Baseline data.

Assays	Baseline	CVF or Switch
PSGT	Y	**Y**
PSIN	N	**Y**
GSIN	N	**Y**
2nd PSGT+IN	**Y**	-

15.6.6. Health Outcomes

HIV Treatment Satisfaction Questionnaire (HIVTSQ)

Questionnaire (Questions 1-10 are scored CCI)

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

Treatment Satisfaction Score

- Total Treatment Satisfaction Score is computed with items 1-10. Items 1-10 are summed to produce a score with a possible range of 0 to 60.
- Higher scores represent greater treatment satisfaction as compared to the past few weeks.
- A maximum of 5 items can be missing, which can be imputed to reflect the mean of the completed item scores. If 6 or more items are missing, then the treatment satisfaction scale score should not be computed.
- General Satisfaction/Clinical sub-score is computed with items CCI and CCI. These items are summed to produce a score with possible range of 0 to 30
- Lifestyle/ease sub-score is computed with items CCI and CCI These items are summed to produce a score with possible range of 0 to 30.

Individual Item Scores

- Items are rated as 6 (CCI, etc.) to 0 CCI, CCI, etc.).
- Higher scores represent greater satisfaction with each aspect of treatment
- For individual item scores outputs, missing scores will not be computed (according to Page 7 of the [HIVTSQ User Guidelines]).
- If multiple assessments equidistant from the target Study Day, the assessments with worst score will be used.

Symptom Distress Module
Questionnaire (Questions 1-20 are scored CCI)
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded. [redacted]

• The Symptom Distress Module (also referred to as HIV Symptom Index) is a 20-item self-reported measure that addresses the presence and perceived distress linked to symptoms commonly associated with HIV or its treatment.
• The aggregate scores are derived from the individual scores:
  • symptom count: unweighted sum of the number of symptoms which are present;
  • symptom bother score: unweighted sum of the bother item scores for each symptom.
• These aggregate scores are considered assessable only if less than 10% of the symptom items (i.e. one or two symptom items) are missing. The missing items are then considered as the "I do not have this symptom" option as this would be interpreted as the symptom was either not applicable or unimportant to the subject.
• If more than two symptoms are missing, the aggregated scores (symptom bother score and symptom count) are set to missing.
• If multiple assessments equidistant from the target Study Day, the assessments with worst score will be used.

Symptom count
• The "symptom count" based on which of the 20 symptoms were present in the subject. • The symptom count ranges from 0 to 20.
Symptom bother score
• The symptom bother score ranges from 0 to 80. • If the subject ticked CCI [redacted], the bother score is 0 • If the subject gave a bother rating, then it is based on ranging from 1 CCI [redacted] to 4 CCI [redacted].

- If the subject ticked two boxes, the worst case is considered. In particular, if the option "I do not have this symptom" is ticked conjointly with a bother rating, the bother score is defined according to the bother rating.

Willingness to switch survey
Questionnaire (Questions 1-7)
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.
• Assess the reason(s) for their participation and facilitate an understanding of subject's willingness to switch • A single item question prior to randomisation. • 7 reasons for willingness to participate in a clinical study where the current HIV medication may be switched check all that apply • Any missing values will remain missing

15.6.7. Cut-off date for protocol deviations

Cut-off date
The following rules should be used to calculate cut-off date for protocol deviations up to and including Week 24: • For subjects who have Week 24 viral load date (cut-off 1): - cut-off = Week 24 viral load date (used for snapshot algorithm) from LB (laboratory) dataset, or date of re-test date if patient had a re-test • For subjects who do not have Week 24 viral load date (cut-off 2): - cut-off date = the earliest of (Day of Study Discontinuation from DS, date of Withdrawal Visit from SV, Study day of permanent treatment discontinuation from EX (for subjects randomized to DTG/3TC) or CM (for patients randomized to CAR), study treatment start date + 210* -1). **upper bound of week 24 window* Additional Statistical Programming Checks to identify 'Subjects with study withdrawal due to a reason of "Protocol Deviation" (as recorded in the eCRF) at or prior Week 24' will be performed. • Consider subjects that have discontinued from the study prior or at Week 24 with 'Protocol deviation' as a reason in DS (study discontinuation). • Cut-off date (cut-off 3): • For subjects who have Week 24 viral load date -> cut-off = Week 24 viral load date (used for snapshot algorithm) from LB (laboratory) dataset. • For subjects who withdrawn before Week 24 Snapshot HIVRNA sample taken or if missing data during week 24 window but on study-> cut-off = IP start date + 210* - 1 • Compare the PD occurrence date (Day of Study Discontinuation from DS) to cut-off date (see paragraph above, please note: cut-off rules 1 and 2 defined above do not apply here) • If cut-off date ≥ PD occurrence date, then deviations will result in exclusion from the per protocol set. *upper bound of week 24 window Similar rules will be followed for Week 48 and subsequent time points and will be detailed in a separate Protocol Deviation specification document. Please refer to latest version of the Protocol Deviation specification document prior to the analysis for full details of protocol deviation identification,

15.6.8. eCRF Baseline Third Agent Class Determination

Baseline third agent will be determined as the third agent ingredient:

- still being taken at randomization for CAR patients
- discontinued immediately prior to randomization for DTG/3TC patients.

15.7. Appendix 7: Reporting Standards for Missing Data

15.7.1. Premature Withdrawals

Element	Reporting Detail
General	Subject study completion (i.e. as specified in the protocol) was defined as: • Randomly assigned to either treatment group, completed the Randomized Phase including the Week 52 visit, and did not enter the Continuation Phase; • Subjects randomized to DTG/3TC treatment group, completed the Randomized Phase including the Week 52 visit, entered and completed the Continuation Phase, defined as remaining on study until: o DTG and 3TC FDC tablet is locally approved for use as a 2-drug regimen, and available through public health services or through the subject's usual health insurance payer, or o the actual FDC tablet, if required by local regulations, is available, or o the subject no longer derives clinical benefit, or o the subject meets a protocol-defined reason for discontinuation, or o development of the DTG/3TC dual regimen is terminated. • Withdrawn subjects will not be replaced in the study. • All available data from subjects who were withdrawn from the study will be listed.

15.7.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data are not provided, leading to blank fields on the collection instrument: • These data will be indicated by the use of a "blank" in subject listing displays. Unless all data for a specific visit are missing in which case the data are excluded from the table. • Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should not be displayed as such.
Snapshot	• In the Snapshot dataset, subjects without HIV-1 RNA data in the assessment window for the visit of interest (due to missing data or discontinuation of IP prior to the visit window) are classified as either 'HIV-1 RNA ≥50 c/mL') or 'No Virologic Data'. For full details of the Snapshot algorithm see Appendix 11
Observed Case (OC)	• This dataset uses only the data that is available at a particular timepoint, with no imputation for missing values.

15.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in subject listing displays. • Where necessary, display macros may impute dates as temporary variables for sorting data in listings only. In addition, partial dates may be imputed for 'slotting' data to study phases or for specific analysis purposes as outlined below.
Exposure	• If study treatment stop date is missing, then for the purposes of calculating exposure, it will be imputed using the date of last visit or the recorded date of withdrawal/completion whichever is earlier. • Partially Missing Stop Day: Last day of the month or last month of the year will be used, unless this is after the stop date of study treatment or withdrawal date; in this case the earliest of the two dates will be used. Note Study Treatment DTG/3TC is recorded on the Study Treatment eCRFs and CAR treatment is recorded on the CONART eCRFs.
Adverse Events and Clinical Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE and Clinical Event start and end dates; that is, the day of the month may be missing: ○ If the full date cannot be ascertained, the following conventions will be applied for calculating the time to onset and the duration of the event: Completely missing dates: (i.e. no year specified) will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing. ○ Partially Missing Start Day: First day of the month or first month of the year will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 4: Treatment States and Phases

Element	Reporting Detail
	○ Partially Missing Stop Day: Last day of the month or last month of the year will be used, unless this is after the stop date of study treatment or withdrawal date; in this case the earliest of the two dates will be used. Otherwise, if patient hasn't withdrawn, last visit date will be used. ○ The recorded partial date will be displayed in listings.
Concomitant Medications	• Partial dates for any concomitant medications recorded in the eCRF will be imputed using the following convention: ○ If the partial date is a start date, the first day of the month will be used for the day and 'Jan' will be used for the month ○ If the partial date is a stop date, last day of the month will be used for the day and 'Dec' will be used for the month. ○ For medications recorded in the eCRF as prior ART, the earlier of this imputed date or the day before IP start will be used. • The recorded partial date will be displayed in listings.

15.8. Appendix 8: Values of Potential Clinical Importance

Element	Reporting Detail
Laboratory Values (Chemistry (Including Lipids), Hematology and Urinalysis)	• The DAIDS grading for severity of laboratory toxicities and clinical adverse events is included in the protocol. • The central laboratory will flag laboratory parameter toxicities directly in the provided datasets for subjects with any value outside normal range. • Abnormalities for potential clinical concern/importance will be defined as any Grade1-5 toxicity.

15.9. Appendix 9: Population Pharmacokinetic (PopPK) Analyses

There is no population pharmacokinetic analysis planned in this study.

15.10. Appendix 10: Time to Event Details

15.10.1. TRDF Detailed Steps

TRDF Detailed steps		
The steps below are for the derivation of TRDF at specific timepoints when the upper bound of the analysis window is used as a cut-off i.e. for the table only. Randomized Period denotes period where subjects are still on their randomized treatment, prior to entering Continuation Phase for DTG/3TC subjects. This is also irrespective of blinding.		
Final step of the derivation is made in following order: [1] When one EVENT (1.2, 2.2, 3.2, 4.2) criterion is satisfied, select. In situations where more than one EVENT criteria satisfied, select the earliest event. If the earliest event date satisfies more than one criteria (e.g. subject had CVW and discontinuation), select CVW. [2] When one CENSOR (1.1, 2.1, 3.1, 4.1, 5.x) criterion is satisfied, select. Else in situations where more than one CENSOR criteria satisfied, select the latest censor day. If the latest event date satisfies more than one criteria, apply the ordering below.		
Condition	**Censor Status**	**Event Description/AVAL**
1. Subjects met CVW event criteria during the randomized period. (Based on derived CVW confirmed prior to cut-off used for the analysis) Then set **tempAVAL**= Study Day of SVW immediately preceding CVW		
1.1 Initial elevation/SVW immediately preceding CVW event date is after the upper bound of the analysis visit window i.e tempAVAL > upper bound of the analysis visit window for Week X	CNSR=1	EVNTDESC=Censored due to data cutoff. AVAL=Upper bound of analysis visit window.

1.2 Initial elevation/SVW immediately preceding CVW event date is on or before the upper bound of the analysis visit window i.e tempAVAL ≤ upper bound of the analysis visit window for Week X	CNSR=0	EVNTDESC=CVW. AVAL= tempAVAL.
2. Subjects with study withdrawal due to treatment related adverse events during the randomized period (defined as subjects that have reason for withdrawal =AE on disposition page and that the subject has at least one AE considered both: i) drug related (AEREL=Y) and ii) result in withdrawal from study (AEWD=Y)) Then set **tempAVAL**= Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study day of permanent treatment discontinuation [from Exposure and Concomitant ART domains]). Assumption: Study day of permanent treatment discontinuation is included in the definition to account for cases where discontinuation information is recorded later. This is a conservative approach consistent with treatment discontinuation preceding withdrawal.		
2.1 Study withdrawal is after the upper bound of the analysis visit window i.e tempAVAL > upper bound of the analysis visit window	CNSR=1	EVNTDESC=Censored due to data cutoff. AVAL=Upper bound of analysis visit window.
2.2 Study withdrawal is on or before the upper bound of the analysis visit window	CNSR=0	EVNTDESC=Study Withdrawal Due to Treatment Related AE. AVAL= tempAVAL

i.e tempAVAL ≤ upper bound of the analysis visit window		
3: Subjects met protocol defined stopping criteria during the randomized period., (Based on disposition page) Then set **tempAVAL**=Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study day of permanent treatment discontinuation [from Study Treatment or CONART eCRF pages]).		
3.1 Protocol defined stopping criteria were met after the upper bound of the analysis visit window i.e tempAVAL > upper bound of the analysis visit window	CNSR=1	EVNTDESC=Censored due to data cutoff. AVAL=Upper bound of analysis visit window.
3.2 Protocol defined stopping criteria were met on or before the upper bound of the analysis visit window i.e tempAVAL ≤ upper bound of the analysis visit window	CNSR=0	EVNTDESC=Study Withdrawal Due to Protocol Defined Criteria. AVAL=tempAVAL
4: Subjects with study withdrawal due to lack of efficacy during the randomized period. (Based on disposition page)		

Then set **tempAVAL**= Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study day of permanent treatment discontinuation [from Study Treatment or CONART eCRF pages])		
4.1 Study withdrawal is after the upper bound of the analysis visit window i.e tempAVAL > upper bound of the analysis visit window	CNSR=1	EVNTDESC=Censored due to data cutoff. AVAL=Upper bound of analysis visit window.
4.2 Study withdrawal is on or before the upper bound of the analysis visit window i.e tempAVAL ≤ upper bound of the analysis visit window	CNSR=0	EVNTDESC=Study Withdrawal Due to Lack of Efficacy AVAL= tempAVAL
If none of the above conditions met		
5: Subjects with study withdrawal for other reasons during the randomized period. (Based on disposition page) Then set **tempAVAL**= Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study day of permanent treatment discontinuation [from Study Treatment or CONART eCRF pages])		
5.1 Study withdrawal is after the upper bound of the analysis visit window	CNSR=1	EVNTDESC=Censored due to data cutoff.

i.e tempAVAL > upper bound of the analysis visit window		AVAL=Upper bound of analysis visit window.
5.2 Study withdrawal is on or before the upper bound of the analysis visit window i.e tempAVAL ≤ upper bound of the analysis visit window	CNSR=1	EVNTDESC=Censored due to Study Discontinuation for Other Reasons. AVAL=tempAVAL
6: Subject completed the randomized period of the study. (Based on disposition page)	CNSR=1	EVNTDESC= Censored as completed the Randomized Period. AVAL= Date of end of Treatment Phase
7: Subject is ongoing in the study during the randomized period and have not yet completed the randomized period Assumption: this will only be in cases where the reporting effort/analysis is performed midway through the randomized period	CNSR=1	EVNTDESC= Censored due to data cutoff. AVAL=Upper bound of analysis visit window.

15.10.2. TRDF Detailed Steps for the Kaplan-Meier plot

TRDF Detailed steps		
The steps below are for the derivation of TRDF overall i.e. for the Kaplan-Meier plot only.		
Final step of the derivation is made in following order: [1] When one EVENT (conditions 1-4) criterion is satisfied, select. In situations where more than one EVENT criteria satisfied, select the earliest event. If the earliest event date satisfies more than one criteria (e.g. subject had CVW and discontinuation), select CVW. [2] When one CENSOR (conditions 5.x) criterion is satisfied, select. Else in situations where more than one CENSOR criteria satisfied, select the latest censor day. If the latest event date satisfies more than one criteria, apply the ordering below.		
Condition	**Censor Status**	**Event Description/AVAL**
1. Subjects met CVW event criteria during the randomized period. (Based on derived CVW confirmed prior to cut-off used for the analysis)	CNSR=0	EVNTDESC=CVW. AVAL=Study Day of SVW immediately preceding CVW.
2. Subjects with study withdrawal due to treatment related adverse events during the randomized period (defined as subjects that have reason for withdrawal =AE on disposition page and that the subject has at least one AE considered both: i) drug related (AEREL=Y) and ii) result in withdrawal from study (AEWD=Y))	CNSR=0	EVNTDESC=Study Withdrawal Due to Treatment Related AE. AVAL=Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study day of permanent treatment discontinuation [from Study Treatment or CONART eCRF pages]).
3: Subjects met protocol defined stopping criteria during the randomized period., (Based on disposition page)	CNSR=0	EVNTDESC=Study Withdrawal Due to Protocol Defined Criteria. AVAL=Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study day of permanent treatment discontinuation

		[from Study Treatment or CONART eCRF pages]).
4: Subjects with study withdrawal due to lack of efficacy during the randomized period. (Based on disposition page)	CNSR=0	EVNTDESC=Study Withdrawal Due to Lack of Efficacy AVAL= Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study day of permanent treatment discontinuation [from Study Treatment or CONART eCRF pages])
If none of the above conditions met		
5: Subjects with study withdrawal for other reasons on or before the end of randomized period. (Based on disposition page)	CNSR=1	EVNTDESC=Censored due to Study Discontinuation for Other Reasons. AVAL=Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study day of permanent treatment discontinuation [from Study Treatment or CONART eCRF pages])
6: Subject completed the randomized period of the study. (Based on disposition page)	CNSR=1	EVNTDESC= Censored as completed the Randomized Period. AVAL= Date of completion of randomized study period
7: Subject is ongoing in the study during the randomized period and have not yet completed the randomized period	CNSR=1	EVNTDESC= Ongoing in the Study. AVAL=Last visit date

Notes:
Randomized Period = Randomized Phase
Efficacy visit windows should be used throughout for the upper bound of the analysis visit window
Subjects are considered to have completed the randomized period if they completed the Randomized Phase.
By definition, a subject must be on-treatment for a CVW to be recorded therefore inclusion of study date of treatment discontinuation in the derivation is not required
EVNTDESC, AVAL & CNSR variables created for the following timepoints:
Week 24 or 48 – for the table analysis
Overall – for the Kaplan-Meier plot

15.10.3. ERDF Detailed Steps

Similar algorithm will be applied for ERDF analyses and Kaplan-Meier figure, where condition 2 and 3 in Section 15.10.1 and Section 15.10.2 will not be considered.

15.11. Appendix 11: Snapshot Algorithm Details

- Consider an analysis visit window, Week X (e.g. Week 24, Week 48). The Window for Week 24/48 visit is defined in Appendix 3. e.g. Week 48 (±6 Week: 295 ≤ Study Day ≤ 378)
- Consider an HIV1-RNA threshold (e.g. 40, 50, 200 copies/mL …) in analysis,
- The analysis window 'Week 48' and HIV1-RNA threshold of '50 c/mL' are used for the purpose of illustration. A subject's Snapshot response and reason at Week 48 are categorized as below.

    - HIV1-RNA < **50** copies/mL
    - HIV1-RNA ≥ **50** copies/mL
        - Data in window not below 50
        - Discontinued for lack of efficacy
        - Discontinued for other reason while not below 50
        - Change in background therapy*
    - No Virologic Data at Week 48 Window
        - Discontinued study due to AE or death
        - Discontinued study for other reasons
        - On study but missing data in window

* Note: since changes in ART or dose modification are not permitted in this protocol, all such subjects who change ART during Randomized Phase will be considered 'HIV1-RNA ≥ 50 c/mL'. if the change in ART is made prior to an analysis timepoint. For subjects on CAR, a switch from a PI boosted with ritonavir to the same PI boosted with cobicistat (and vice versa) is permitted per protocol and a switch from lamivudine to emtricitabine and vice versa will not be considered 'HIV1-RNA ≥ 50 copies/mL' due to 'change in ART'.

The steps in determining response and reasons are indicated in Table below, in the order stated.

Detailed steps		
• Please note that the following scenarios will NOT be penalized Per Snapshot algorithm (i.e. please excluding these scenarios from **Condition** 1-4). • Dose reduction, dropping a component, or change in formulation (e.g. 'Tivicay + Kivexa' to 'Triumeq' with the identical ingredients) • Permitted Change (if a decision date is not collected in eCRF) / decision to permitted change is made prior to/on the first on-treatment viral load result • Permitted change is made after the first on-treatment viral load result AND last on-treatment viral load prior to/on the date of change is <50 c/mL		
Condition ('Week 48' indicates Week 48 window)	**Response**	**Reasons**

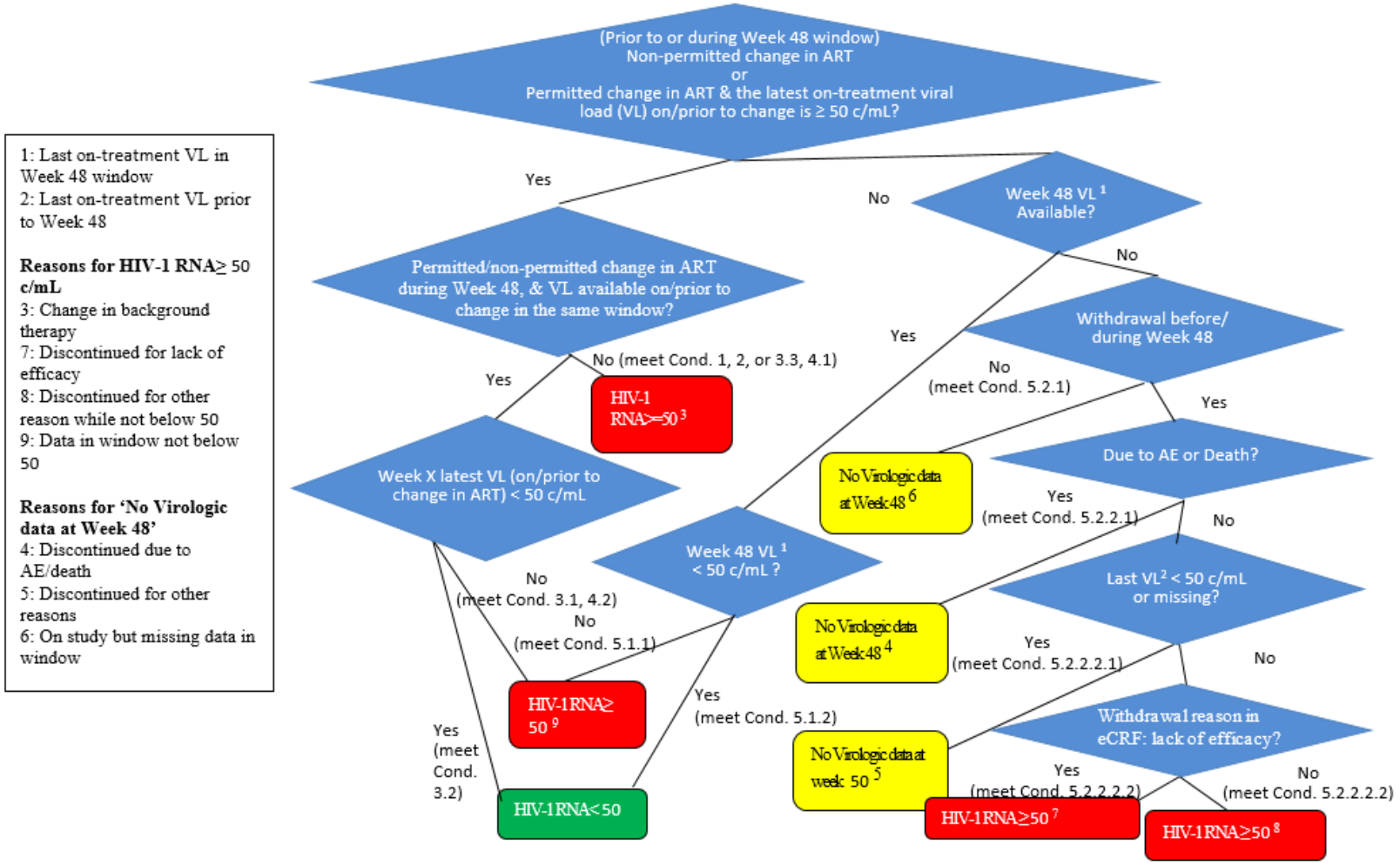
1. If ***non-permitted*** change in background therapy ***prior to*** Week 48	HIV1-RNA ≥ 50	Change in background therapy
2. If ***permitted*** change in background therapy ***prior to*** Week 48 AND the latest on-treatment VL prior to/on the date of change is ≥ 50 c/m [a]	HIV1-RNA ≥ 50	Change in background therapy
3. If ***non-permitted*** change in background therapy ***during*** Week 48		
• 3.1 Last on-treatment VL during Week 48 prior to/on the date of change ≥ 50 c/mL	HIV1-RNA ≥ 50	Data in window not below 50
• 3.2 Last on-treatment VL during Week 48 prior to/on the date of change <50 c/mL	HIV1-RNA < 50	
• 3.3 No VL during Week 48 prior to/on the date of change	HIV1-RNA ≥ 50	Change in background therapy
4. If ***permitted*** change in background therapy ***during*** Week 48 AND the last on-treatment VL prior to/on the date of change is ≥ 50 c/mL [a]		
4.1 this last on-treatment VL occurs prior to Week 48	HIV1-RNA ≥ 50	Change in background therapy
4. 2 this last on-treatment VL occurs during Week 48 but prior to/on the date of change	HIV1-RNA ≥ 50	Data in window not below 50
5. If none of the above conditions met		
5.1 VL available during Week 48		
5.1.1 Last on-treatment VL during Week 48 ≥ 50 c/mL	HIV1-RNA ≥ 50	Data in window not below 50
5.1.2 Last on-treatment VL during Week 48 <50 c/mL	HIV1-RNA < 50	
5.2 No VL during Week 48		
5.2.1 If subjects still on study (i.e. The on-treatment period has not been ended up to the upper bound of Week 48 window. For example, for oral treatment, the on-treatment period ends at permanently IP stop date+1)	No virologic data at Week 48 Window	On study but missing data in window
5.2.2 If subjects withdraw before/during Week 48 due to :-		
5.2.2.1 Safety reasons (e.g. AE/death, liver chemistry stopping criteria, renal toxicity withdrawal criteria, QTc withdrawal criteria et al, as recorded in eCRF Study Conclusion form)	No virologic data at Week 48 Window	Disc. due to AE/death
5.2.2.2 Non-safety related reasons (e.g. Lack of efficacy, protocol deviation, withdrew consent, loss to follow-up, study closed/terminated,		

investigator discretion et al, as recorded in eCRF Study Conclusion Form)		
5.2.2.2.1 Last on-treatment VL <50 c/mL OR no on-treatment VL available during study	No virologic Data at Week 48 Window	Disc. for other reasons
5.2.2.2.2 Last on-treatment VL ≥ 50 c/mL AND withdrawal due to Lack of efficacy	HIV1-RNA ≥ 50	Disc. for lack of efficacy
5.2.2.2.3 Last on-treatment VL ≥ 50 c/mL AND withdrawal due to all other non-safety related reasons	HIV1-RNA ≥ 50	Disc. for other reason while not below 50

[a]: Excluding permitted change in background therapy where change or decision to change is made prior to/on the first on-treatment viral result

Snapshot outcomes are shown below and are to be used in conjunction with the steps in the Snapshot algorithm

Figure 1 Flowchart of Snapshot Outcome



A dataset will be created based on the Snapshot algorithm, where the dataset contains the following information, as a minimum:

Study identification

Subject identification

Study day and date of last blinded treatment

Virologic outcome based on the snapshot approach (i.e., HIV-1 RNA < 50 c/mL, HIV-1 RNA ≥ 50 c/mL, discontinued due to AE or death, discontinued for other reasons, on study but missing data during window)

The HIV-1 RNA measurement and the corresponding study day and date used to determine the above virologic outcome if the measurement was not missing

Study day and date when the subject switched to open-label treatment due to lack or loss of virologic suppression, if applicable

Discontinuation study day and date, reason for discontinuation, and last blinded treatment measurement before discontinuation for subjects who discontinued study drug

15.12. Appendix 12: Modified Snapshot Algorithm Details

The below Modified Snapshot Algorithm will be used to determine Snapshot outcomes taking into account COVID-19 related events. The Modified Snapshot Estimand still reports high-level categories (>=50 c/mL, <50 c/mL and No Virologic Data) in exactly the same way as the standard FDA Snapshot Algorithm in Section 15.11, however it reports additional subcategories to account for outcomes related to COVID-19.

- Consider an analysis visit window, Week X (e.g. Week 24, Week 48). The Window for Week 24/48 visit is defined in Appendix 3. e.g. Week 48 (±6 Week: 295 ≤ Study Day ≤ 378)
- Consider an HIV1-RNA threshold (e.g. 40, 50, 200 copies/mL …) in analysis,
- The analysis window 'Week 48' and HIV1-RNA threshold of '50 c/mL' are used for the purpose of illustration. A subject's Modified Snapshot response and reason at Week 48 are categorized as below.

    - HIV1-RNA < **50** copies/mL
    - HIV1-RNA ≥ **50** copies/mL
      Data in window not below 50
      Non-COVID-19 related
        Discontinued for lack of efficacy
        Discontinued for other reason and HIV-1 RNA >= 50 copies/mL
        Change in ART*
      COVID-19 related
        Discontinued for lack of efficacy
        Discontinued for other and HIV-1 RNA >= 50 copies/mL
        Change in background therapy*

    - No Virologic Data at Week 48 Window
      Non COVID-19 related
        Discontinued study due to AE or death
        Discontinued study for other reasons
        On study but missing data in window
      COVID-19 related
        Discontinued study due to AE or death
        Discontinued study for other reasons
        On study but missing data in window

* Note: since changes in ART or dose modification are not permitted in this protocol, all such subjects who change ART during Randomized Phase will be considered 'HIV1-RNA ≥ 50 c/mL' if the change in ART is made prior to an analysis timepoint. For subjects on CAR, a switch from a PI boosted with ritonavir to the same PI boosted with cobicistat (and vice versa) is permitted per protocol and a switch from lamivudine to emtricitabine and vice versa will not be considered 'HIV1-RNA ≥ 50 copies/mL' due to 'change in ART'.

The steps in determining response and reasons are indicated in Table below, in the order stated.

Detailed steps

- Please note that the following scenarios will NOT be penalized Per Modified Snapshot algorithm (i.e. please excluding these scenarios from Condition 1-4).
- Dose reduction, dropping a component, or change in formulation (e.g. 'Tivicay + Kivexa' to 'Triumeq' with the identical ingredients)
- Permitted Change (if a decision date is not collected in eCRF) / decision to permitted change is made prior to/on the first on-treatment viral load result
- Permitted change is made after the first on-treatment viral load result AND last on-treatment viral load prior to/on the date of change is <50 c/mL

Condition ('Week 48' indicates Week 48 window)	**Response**	**Reasons**
1.1 If ***non-permitted*** change in background therapy ***prior to*** Week XX (Non-COVID-19 switch)	HIV1-RNA ≥ 50	Change in background therapy (Non-COVID-19 related)
1.2 If ***non-permitted*** change in background therapy ***prior to*** Week XX (COVID-19 switch)	HIV1-RNA ≥ 50	Change in background therapy (COVID-19 related)
2. 1 If ***permitted*** change in background therapy ***prior to*** Week 48 AND the latest on-treatment VL prior to/on the date of change is ≥ 50 c/mL (not related to COVID-19) [a]	HIV1-RNA ≥ 50	Change in background therapy(Non-COVID-19 related)
2. 2 If ***permitted*** change in background therapy ***prior to*** Week 48 AND the latest on-treatment VL prior to/on the date of change is ≥ 50 c/mL(related to COVID-19) [a]	HIV1-RNA ≥ 50	Change in background therapy(COVID-19 related)
4. If ***non-permitted*** change in background therapy ***during*** Week 48		
• 3.1 Last on-treatment VL during Week 48 prior to/on the date of change ≥ 50 c/mL	HIV1-RNA ≥ 50	Data in window not below 50
• 3.2 Last on-treatment VL during Week 48 prior to/on the date of change <50 c/mL	HIV1-RNA < 50	
• 3.3.1 No VL during Week 48 prior to/on the date of change (non-related to COVID-19)	HIV1-RNA ≥ 50	Change in background therapy(Non-COVID-19 related)
• 3.3.2 No VL during Week 48 prior to/on the date of change (related to COVID-19)	HIV1-RNA ≥ 50	Change in background therapy(COVID-19 related)

5. If ***permitted*** change in background therapy ***during*** Week 48 AND the last on-treatment VL prior to/on the date of change is ≥ 50 c/mL [a]		
4.1.1 this last on-treatment VL occurs prior to Week 48 (non- COVID-19 related switch)	HIV1-RNA ≥ 50	Change in background therapy (Non-COVID-19 related)
4.1.2 this last on-treatment VL occurs prior to Week 48 (COVID-19 related switch)	HIV1-RNA ≥ 50	Change in background therapy (COVID-19 related)
4. 2 this last on-treatment VL occurs during Week 48 but prior to/on the date of change	HIV1-RNA ≥ 50	Data in window not below 50
5. If none of the above conditions met		
5.1 VL available during Week 48		
5.1.1 Last on-treatment VL during Week 48 ≥ 50 c/mL	HIV1-RNA ≥ 50	Data in window not below 50
5.1.2 Last on-treatment VL during Week 48 <50 c/mL	HIV1-RNA < 50	
5.2 No VL during Week 48		
5.2.1 Participants unable to attend Week 48 visit due to COVID-19, but otherwise considered still on-study (i.e. The on-treatment period continues beyond the upper bound of Week 48 window. For example, for oral treatment, a participant with IP stop date+1> Day 378 of the upper bound of Week 48 window, would be considered 'on study' for Week 48 snapshot assessment)	No virologic data at Week 48 Window	On study but missing data in window(COVID-19 related)
5.2.2 If participants still on study but participant has not missed visit due to COVID-19 (i.e. The on-treatment period continues beyond the upper bound of Week 48 window. For example, for oral treatment, a participant with IP stop date+1> Day 378 of the upper bound of Week 48 window, would be considered 'on study' for Week 48 snapshot assessment)	No virologic data at Week 48 Window	On study but missing data in window(Non-COVID-19 related)
5.3.2 If participants withdraw before/during Week 48 due to:		
5.3.2.1 Non-COVID-19 Safety reasons (e.g. non-COVID-19 AE/death, liver chemistry stopping criteria, renal toxicity withdrawal criteria, QTc withdrawal criteria, as recorded in eCRF Conclusion form)	No virologic data at Week 48 Window	Disc. due to AE/death(Non-COVID-19 related)

5.3.2.2 COVID-19 safety reasons eCRF (e.g. AE/death resulting from COVID-19 as recorded in the eCRF Conclusion form). If subject has AE or death recorded as primary reason for discontinuing (not captured as COVID-19 related), but subject has at least one COVID-19 related AE/death leading to withdrawal per AE eCRF page, the subject will assumed to have discontinued as a result of COVID-19 AE/death and hence will be captured in this Snapshot category.	No virologic data at Week 48 Window	Disc. due to AE/death(COVID-19 related)
5.3.2.3 Non-safety and non-COVID-19 related reasons (e.g. Lack of efficacy, protocol deviation, withdrew consent, loss to follow-up, study closed/terminated, investigator discretion et al, as recorded in eCRF Study Conclusion Form)		
5.3.2.3.1 Last on-treatment VL <50 c/mL OR no on-treatment VL available during study	No virologic Data at Week 48 Window	Disc. for other reasons(Non-COVID-19 related)
5.3.2.3.2 Last on-treatment VL ≥ 50 c/mL AND withdrawal due to Lack of efficacy	HIV1-RNA ≥ 50	Disc. for lack of efficacy(Non-COVID-19 related)
5.3.2.3.3 Last on-treatment VL ≥ 50 c/mL AND withdrawal due to all other non-safety related reasons	HIV1-RNA ≥ 50	Disc. for other reason while not below 50(Non-COVID-19 related)
5.3.2.4 Non-safety and COVID-19 related reasons (e.g. Withdrawal of consent, protocol deviation (where subreason is COVID-19), investigator discretion (where Other text is recorded as 'COVID-19'), as recorded in eCRF Conclusion Form)		
5.3.2.4.1 Last on-treatment VL <50 c/mL OR no on-treatment VL available during study	No virologic Data at Week 48 Window	Disc. for other reasons(COVID-19 related)
5.3.2.4.2 Last on-treatment VL ≥ 50 c/mL AND withdrawal due to all other non-safety related reasons	HIV1-RNA ≥ 50	Disc. for other reason while not below 50(COVID-19 related)

15.13. Appendix 13: Abbreviations & Trade Marks

15.13.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
CAR	Current ART regimen
cART	Combination ART
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DOB	Date of Birth
DP	Decimal Places
DOV	Date of Visit
eCRF	Electronic Case Record Form
ERDF	Efficacy Related Discontinuation Failure
IA	Interim Analysis
ICH	International Conference on Harmonisation
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
IMMS	International Modules Management System
IP	Investigational Product
ITT	Intent-To-Treat
GUI	Guidance
LOC	Last Observation Carries Forward
MMRM	Mixed Model Repeated Measures
PCI	Potential Clinical Importance
PD	Protocol Deviation
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RAMOS	Randomization & Medication Ordering System
SAC	Statistical Analysis Complete
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
TA	Therapeutic Area
TAF	Tenofovir alafenamide fumarate

Abbreviation	Description
CAR	Current antiretroviral regimen
TFL	Tables, Figures & Listings
TRDF	Treatment Related Discontinuation Failure
GSK	GlaxoSmithKline

15.13.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
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Tivicay

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Monogram Inc
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WinNonlin

15.14. Appendix 14: Model Checking and Diagnostics for Statistical Analyses

15.14.1. Statistical Analysis Assumptions

Endpoint(s)	Change from Baseline in bone/renal/inflammatory biomarkers, weight, BMI, HOMA-IR, HbA1c, lipids and health outcomes
Analysis	MMRM/ANCOVA

- Model assumptions will be applied, but appropriate adjustments maybe made based on the data.
- The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used for MMRM models.
- An unstructured covariance structure for the R matrix will be estimated by treatment group by specifying 'type=UN' and 'group=treat' on the REPEATED line for MMRM models.
    - In the event that this model fails to converge, alternative correlation structures may be considered such as CSH or CS.
    - Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure.
- Distributional assumptions underlying the model used for analysis will be examined by obtaining a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable.
- If there are any departures from the distributional assumptions, alternative models will be explored using appropriate transformed data.

Endpoint(s)	Change from Baseline in Lipids
Analysis	Multiple Imputation

- Model assumptions will be applied, but appropriate adjustments maybe made based on the data.
- Distributional assumptions underlying the model used for analysis will be examined by obtaining a normal probability plot of the residuals (i.e. checking the normality assumption) to gain confidence that the model assumptions are reasonable.
- If there are any departures from the distributional assumptions, alternative models will be explored using appropriate transformed data.
- Diagnostic plots (trace and autocorrelation plots) will be checked to verify that the number of burn-in iterations and MCMC steps between imputed datasets are sufficient. If the trace plots show apparent trend or the autocorrelation plots show significant positive or negative autocorrelation, number of iterations will be increased until the diagnostic plots are acceptable.
- .

15.15. Appendix 15: Test of Homogeneity: Fleiss, Liu & Kelly Method

15.15.1. Statistical Analysis Method for Test of Homogeneity by Fleiss, Liu & Kelly

Analysis	Test of Homogeneity by Fleiss, Liu & Kelly

Subgroup i (i= 1 to K categories)

$Treatment_j$ (j=1,2)	Outcome of Interest	Not Outcome of Interest	Total
Non-Sparse cells (If both $\hat{\pi}_{i1}$ or $\hat{\pi}_{i2}$ (proportion of outcome in either treatment for level i) is not 0 or 1 no modification is made to counts of outcome):			
$Trt_j=Trt_1$	$x_{ij} = x_{11}$	$n_{ij} - x_{ij} = n_{11} - x_{11}$	$n_{ij} = n_{11}$
$Trt_j=Trt_2$	$x_{ij} = x_{12}$	$nij - xij = n_{12} - x_{12}$	$n_{ij} = n_{12}$
Sparse cells: If either $\hat{\pi}_{i1}$ or $\hat{\pi}_{i2}$ (proportion of outcome in either treatment for level i) is 0 or 1 add 0.5 to each cell in level i (for level i only)			
$Trt_j=Trt_1$	$x_{ij} = x_{11} + 0.5$	$n_{11} - x_{11} + 0.5$	$n_{ij} = n_{11} + 1$
$Trt_j=Trt_2$	$x_{ij} = x_{12} + 0.5$	$n_{12} - x_{12} + 0.5$	$n_{ij} = n_{12} + 1$

$$\hat{\pi}_{ij} = \frac{x_{ij}}{n_{ij}}$$

H0: Risk differences in each level are equal.

Test Statistic: $Q_{wls} = \sum_{i=1}^{K} \frac{(Y_i - \hat{\tau})^2}{\hat{w}_I} \sim ChiSq_{(K-1)}$

$$Y_i = \hat{\pi}_{i1} - \hat{\pi}_{i2}$$

$$\hat{\tau} = \frac{\sum_{i=1}^{K} \frac{Y_i}{\hat{w}_i}}{\sum_{i=1}^{K} \frac{1}{\hat{w}_i}}$$

$$w_i = \frac{\hat{\pi}_{i1}(1-\hat{\pi}_{i1})}{n_{i1}-1} + \frac{\hat{\pi}_{i2}(1-\hat{\pi}_{i2})}{n_{i2}-1}$$

15.16. Appendix 16: List of Data Displays

15.16.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.01 to 1.n	1.01 to 1.n
Efficacy	2.01 to 2.n	2.01 to 2.n
Safety	3.01 to 3.n	3.01 to 3.n
Virology	4.01 to 4.n	4.01 to 4.n
Pharmacokinetic	5.01 to 5.n	5.01 to 5.n
Health Outcomes	6.01 to 6.n	6.01 to 6.n
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	y to z	

15.16.2. Mock Example Shell Referencing

Non- GSK Statistical Display Standard specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 17: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Population Pharmacokinetic (PopPK)	POPPK_Fn	POPPK_Tn	POPPK_Ln
Pharmacodynamic and / or Biomarker	PD_Fn	PD_Tn	PD_Ln
Pharmacokinetic / Pharmacodynamic	PKPD_Fn	PKPD_Tn	PK/PD_Ln

NOTES:

- Non-Standard displays are indicated in the 'GSK Statistical Display Standard/ Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

15.16.3. Deliverables

Delivery [Priority] [1]	Description
DS [X]	During Study
IA SAC [X]	Interim Analysis Statistical Analysis Complete
SAC [X]	Final Statistical Analysis Complete

NOTES:

1. Indicates priority (i.e. order) in which displays will be generated for the reporting effort

15.16.4. Study Population Tables

Note that where the Deliverable column states 'All', this refers to all reporting efforts i.e. Weeks 24 and 48.

Study Population Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	ITT-E	ES1	Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic	ICH E3, FDAAA, EudraCT Present by "Not Related to COVID-19" and " Related to COVID-19" and Overall	All
1.2.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements	All
1.3.	Screened	NS1	Summary of Number of Subjects Enrolled by Country and Site ID	EudraCT/Clinical Operations Repeat by ITT-E population for Disclosure purpose. Add Table 1.3.1	All
1.4.	ITT-E	POP_T1	Summary of Reasons for Withdrawal by Visit	ICH E3	All
1.5.	ITT-E	POP_T13	Summary of Misrandomized Strata or Treatment		All
1.6.	ITT-E	POP_T9	Summary of Number of Subjects Attending Nominal and Actual Analysis Visits		All

Study Population Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Protocol Deviation					
1.7.	ITT-E	DV1	Summary of Important Protocol Deviations by Relationship to COVID-19	ICH E3 Present by "Not Related to COVID-19" and " Related to COVID-19" and Overall	All
1.8.	ITT-E	DV1	Summary of Protocol Deviations Leading to Exclusion from the Per-Protocol Population	GSK Statistical Display Standard	All
1.9.				Will be combined with Table 1.7	
Population Analysed					
1.10.	Screened	SP1	Summary of Study Populations	GSK Statistical Display Standard	All
Demographic and Baseline Characteristics					
1.11.	ITT-E	DM1	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	All
1.12.	Screened	DM11	Summary of Age Ranges	EudraCT	All
1.13.				No longer required as it is part of 1.14	
1.14.	ITT-E	DM6	Summary of Race and Racial Combinations Details	ICH E3, FDA, FDAAA, EudraCT	All
1.15.	ITT-E	BASELINE3	Summary of Hepatitis Status at Entry		All
1.16.	ITT-E	CDC1	Summary of CDC Classification of HIV Infection at Baseline		All
1.17.	ITT-E	RF1	Summary of HIV Risk Factors		All

Study Population Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.18.	ITT-E	BASELINE4	Summary of Screening and Baseline Cardiovascular Risk Assessments	GSK Statistical Display Standard	All
1.19.	ITT-E	BASELINE2	Summary of Distribution of CD4+ Cell Count (cells/mm^3) Results at Screening and Baseline		All
1.20.	ITT-E	BASELINE1	Summary of Distribution of Quantitative Plasma HIV-1 RNA Results at Baseline		All
Prior and Concomitant Medications, Medical Conditions					
1.21.	ITT-E	MH1	Summary of Current Medical Conditions	ICH E3	All
1.22.	ITT-E	MH1	Summary of Past Medical Conditions	ICH E3	All
1.23.	ITT-E	CM1	Summary of Concomitant Medications by Ingredient ATC Level 1	ICH E3	All
1.24.	ITT-E	CA1	Summary of Antiretroviral Therapy Stopped Prior to Screening		All
1.25.	ITT-E	CA1	Summary of Antiretroviral Therapy Received at Screening		All
1.26.				Covered in 1.25	
1.27.	ITT-E	CA1	Summary of On-Treatment Antiretroviral Therapy Starting after Day 1		All
1.28.	ITT-E	CA1	Summary of Antiretroviral Therapy Starting after Treatment Discontinuation		All

Study Population Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.29.				Covered in 1.28	
1.30.	ITT-E	CA2	Summary of Baseline Third Agent Class		All
1.31.	ITT-E	POP_T12	Summary of Time since First Antiretroviral Therapy until Day 1		All
1.32.	ITT-E	POP_T7	Summary of History of Depression and Anxiety at Baseline		All
Impact of COVID-19 Pandemic					
1.33.	ITT-E	PAN4	Summary of Visits impacted by COVID-19 Pandemic		All
1.34.	ITT-E	SD4	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment by Relationship to COVID-19 Pandemic	Summarise by: • Related to COVID-19 Not related to COVID-19	All
1.35.	Screened	NS1	Summary of Recruitment by Country and Site Before & After Implementation of Pandemic Measures	The dates when implementation of pandemic measures began will be available in HARP dataset and should be used to define before & after implementation of pandemic measures	All

15.16.5. Study Population Figures

Impact of COVID-19 Pandemic : Figures					
No.	**Population**	**GSK Statistical Display Standard/ TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Visits impacted by COVID-19 Pandemic					
1.1.	ITT-E	PAN8	Visits impacted by COVID-19 Pandemic		All

15.16.6. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Primary Efficacy Analysis					
2.1.	ITT-E	EFF_T1	Summary of Analysis for Percent of Subjects with Plasma HIV-1 RNA ≥ 50 c/mL at Week X – Snapshot Analysis		All
2.2.	Per-Protocol	EFF_T1	Summary of Analysis for Percent of Subjects with Plasma HIV-1 RNA ≥ 50 c/mL at Week X – Snapshot Analysis		All
2.3.	ITT	EFF_T1	Summary of Analysis for Percent of Subjects with Plasma HIV-1 RNA ≥ 50 c/mL at Week X – Snapshot Analysis		All
2.4.	ITT-E	EFF_T1	Summary of Analysis for Percent of Subjects with Plasma HIV-1 RNA ≥ 50 c/mL at Week X – Snapshot Analysis (Sparse Data Sensitivity Analysis)		All

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Secondary Efficacy Analyses					
2.5.	ITT-E	EFF_T1	Summary of Analysis for Percent of Subjects with Plasma HIV-1 RNA <50 c/mL at Week X – Snapshot Analysis		All
2.6.	ITT-E	EFF_T2	Summary of Study Outcomes (Plasma HIV-1 RNA ≥ / < 50 c/mL) at Week X – Snapshot Analysis		All
2.7.	Per-Protocol	EFF_T2	Summary of Study Outcomes (Plasma HIV-1 RNA ≥ / < 50 c/mL) at Week X – Snapshot Analysis		All
2.8.	ITT	EFF_T2	Summary of Study Outcomes (Plasma HIV-1 RNA ≥ / < 50 c/mL) at Week X – Snapshot Analysis		All
2.9.	ITT-E	EFF_T2a	Summary of Study Outcomes (Plasma HIV-1 RNA ≥ / < 50 c/mL) at Week X – Modified Snapshot Analysis		All
2.10.	ITT-E	EFF_T5	Summary of Percent of Subjects with Plasma HIV-1 RNA ≥50 c/mL by Visit – Snapshot Analysis		All
2.11.	ITT-E	EFF_T5	Summary of Percent of Subjects with Plasma HIV-1 RNA <50 c/mL by Visit – Snapshot Analysis		All
2.12.	ITT-E	EFF_T6	Summary of Percent of Subjects with Plasma HIV-1 RNA <50 c/mL at Week X by Subgroup – Snapshot Analysis		All
2.13.	ITT-E	EFF_T3	Summary of Study Outcomes (Plasma HIV-1 RNA ≥ / < 50 c/mL) at Week X by Subgroup - Snapshot Analysis		All
2.14.	ITT-E	EFF_T8	Summary of Change from Baseline in Plasma HIV-1 RNA (log10 c/mL) by Visit		All

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.15.	ITT-E	EFF_T9	Summary of Change from Baseline in in CD4+ count (cells/mm3) by Visit		All
2.16.	ITT-E	EFF_T9	Summary of Change from Baseline in in CD4+/CD8+ count ratio (cells/mm3) by Visit		All
2.17.	ITT-E	EFF_T14	Summary of Change from Baseline in CD4+/CD8+ Count Ratio (cells/mm3) at Week X by Subgroup		All
2.18.	ITT-E	EFF_T10	Summary of Post-Baseline HIV-1 Associated Conditions Including Recurrences		All
2.19.	ITT-E	EFF_T10	Summary of Post-Baseline HIV-1 Associated Conditions Excluding Recurrences		All
2.20.	ITT-E	EFF_T11	Summary of Post-Baseline HIV-1 Disease Progressions		All
2.21.	ITT-E	EFF_T12	Cumulative Proportion of Subjects Meeting Confirmed Virologic Withdrawal Criteria by Visit		All
2.22.	ITT-E	EFF_T13	Distribution of Quantitative Plasma HIV-1 RNA Results at Suspected and Confirmed Virologic Withdrawal		All
2.23.	ITT-E	EFF_T14	Summary of Change from Baseline in in CD4+ count (cells/mm3) at Week X by Subgroup		All
2.24.	ITT-E	EFF_T15	Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Withdrawal at Week X - Treatment Related Discontinuation = Failure		All
2.25.	ITT-E	EFF_T15	Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Withdrawal at Week X - Efficacy Related Discontinuation = Failure		All

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.26.	ITT-E	EFF_T1	Summary of Analysis for percent of Subjects with Plasma HIV-1 RNA <40 c/mL at Week X – Snapshot Analysis		All
2.27.	ITT-E	EFF_T1	Summary of Analysis for Percent of Subjects with Plasma HIV-1 RNA <40 c/mL and Target Not Detected Status at Week X - Snapshot Analysis - ITT-E		All
2.28.	ITT-E	EFF_T5	Summary of Percent of Subjects with Plasma HIV-1 RNA <40 c/mL by Visit - Snapshot Analysis		All
2.29.	ITT-E	EFF_T5	Summary of Percent of Subjects with Plasma HIV-1 RNA <40 c/mL and Target Not Detected Status by Visit - Snapshot Analysis		All
2.30.	ITT-E	EFF_T2	Summary of Study Outcomes (<40 c/mL and Target Not Detected Status) at Week X - Snapshot		All
2.31.	ITT-E	EFF_T6	Summary of Percent of Subjects with Plasma HIV-1 RNA <40 c/mL and Target Not Detected Status at Week X by Baseline Third Agent Class -Snapshot Analysis - ITT-E		All
2.32.	ITT-E	EFF_T2	Summary of Study Outcomes (<40 c/mL) at Week X - Snapshot		

15.16.7. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Secondary Efficacy Analyses					
2.1.	ITT-E	EFF_F2	Unadjusted Treatment Difference in Percent (95% CI) of Subjects with HIV-1 RNA <50 c/mL at Week X by Subgroup – Snapshot Analysis		All
2.2.	ITT-E	EFF_F3	Individual Plasma HIV-1 RNA and CD4+ Profiles by Visit for subjects with at least one viral load ≥50 c/mL		All
2.3.	ITT-E	EFF_F4	Kaplan-Meier Plot of Time to Failure - Treatment Related Discontinuation = Failure (TRDF)		All
2.4.	ITT-E	EFF_F4	Kaplan-Meier Plot of Time to Failure - Efficacy Related Discontinuation = Failure (ERDF)		All

15.16.8. Safety Tables

Safety: Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure					
3.1.	Safety	SAFE_T1	Summary of Extent of Exposure Study Treatment- Randomized Phase	ICH E3	All
Adverse Events					
3.2.	Safety	AE1	Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3	All
3.3.	Safety	AE5B	Summary of Adverse Events by System Organ Class, Maximum Toxicity and Subgroups		All
3.4.	Safety	AE5A	Summary of All Adverse Events by Maximum Grade	ICH E3	All
3.5.	Safety	AE3	Summary of Common (>=2%) Adverse Events by Overall Frequency	ICH E3	All
3.6.	Safety	AE3	Summary of Common (>=2%) Grade 2-5 Adverse Events by Overall Frequency	ICH E3	All
3.7.	Safety	AE1	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term	ICH E3	All
3.8.	Safety	AE5A	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term and Maximum Grade	ICH E3	All

Safety: Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.9.	Safety	AE15	Summary of Common (>=2%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subject and Occurrences)	FDAAA, EudraCT	All
3.10.	Safety	AE3	Summary of Common (>=0.5%) Drug-Related Grade 2-5 Adverse Events by Overall Frequency	ICH E3	All
3.11.	Safety	SAFE_T16	Summary of Subjects with Any Adverse Events by Visit		All
3.12.	Safety	AE20	Summary of Serious Fatal and Non-Fatal Drug-Related Adverse Events by Overall Frequency	Plain Language Summary requirements	All
Serious and Other Significant Adverse Events					
3.13.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT	All
3.14.	Safety	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term /by Overall Frequency	GSK Statistical Display Standard	All
3.15.	Safety	AE5A	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by Maximum Grade		All

Safety: Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.16.	Safety	AE1	Summary of Serious Drug-Related Adverse Events by System Organ Class	Plain Language Summary requirements.	All
3.17.	Safety	SAFE_T2	Summary of Cumulative Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by Visit		All
Impact of Covid-19 on Assessment of Safety Based on COVID-19 eCRF					
3.18.	Safety	PAN1	Number of Subjects with an Adverse Event of Suspected, Probable, Confirmed for COVID-19 Infection	GSK Statistical Display Standard	All
3.19.				Covered in 3.18	
Laboratory: Chemistry					
3.20.	Safety	LB1	Summary of Chemistry Changes from Baseline by Visit	ICH E3	All
3.21.	Safety	SAFE_T17	Summary of Chemistry by Visit	ICH E3	All
3.22.	Safety	SAFE_T13	Summary of AST, ALT and Total Bilirubin Maximum Post-Baseline Emergent Toxicity by Baseline Hepatitis C Status	ICH E3	All
3.23.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting	GSK Statistical Display Standard	

Safety: Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Lipids					
3.24.	Safety	LB1	Summary of Fasting Lipids by Visit	display both mmol/L and mg/DL	All
3.25.	Safety	LB1	Summary of Change from Baseline in Fasting Lipids by Visit	display both mmol/L and mg/DL	All
3.26.	Safety	SAFE_T5	Summary of Changes in NCEP Lipid Baseline Category to Week X Category-Shift Table	display both mmol/L and mg/DL	All
3.27.	Safety	SAFE_T7b	Statistical Analysis of Change from Baseline in Fasting Lipids at Week X - Multiple Imputed Loge Transformed Data - MAR	display both mmol/L and mg/DL	All
3.28.	Safety	SAFE_T7b	Statistical Analysis of Change from Baseline in Fasting Lipids at Week X - Loge Transformed Data – MMRM/ANCOVA	display both mmol/L and mg/DL ANCOVA-Week 24 MMRM-Week 48	All

Safety: Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Hematology					
3.29.	Safety	LB1	Summary of Hematology Changes from Baseline by Visit	ICH E3	All
3.30.	Safety	SAFE_T17	Summary of Hematology by Visit		All
Laboratory: Urinalysis					
3.31.	Safety	LB1	Summary of Urinalysis Changes from Baseline by Visit	ICH E3	All
3.32.	Safety	SAFE_T17	Summary of Urinalysis by Visit		All
Laboratory: Hepatobiliary (Liver)					
3.33.	Safety	LIVER10	Summary of Subjects Meeting Hepatobiliary Abnormality Criteria – All Post-Baseline Abnormalities	GSK Statistical Display Standard	All
Biomarkers (Bone, Renal and Inflammatory)					
3.34.	Safety	LB1	Summary of Change from Baseline in Bone Biomarkers by Visit		All
3.35.	Safety	LB1	Summary of Change from Baseline in Renal Biomarkers by Visit		All
3.36.	Safety	LB1	Summary of Change from Baseline in Renal Biomarkers by Visit- Loge Transformed Data		All
3.37.	Safety	LB1	Summary of Change from Baseline in Inflammatory Biomarkers - Loge Transformed Data		All

Safety: Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.38.	Safety	SAFE_T7b	Statistical Analysis of Change from Baseline Bone Biomarkers at Week X – MMRM/ANCOVA	ANCOVA-Week 24 MMRM-Week 48	All
3.39.	Safety	SAFE_T7a	Statistical Analysis of Change from Baseline in Renal Biomarkers at Week X – MMRM/ANCOVA	ANCOVA-Week 24 MMRM-Week 48	All
3.40.	Safety	SAFE_T7b	Statistical Analysis of Change from Baseline in Renal Biomarkers at Week X - Loge Transformed Data - MMRM /ANCOVA	ANCOVA-Week 24 MMRM-Week 48	All
3.41.	Safety	SAFE_T7b	Statistical Analysis of Change from Baseline in Inflammatory Biomarkers at Week X - Loge Transformed Data – MMRM/ANOCVA	ANCOVA-Week 24 MMRM-Week 48	All
Weight, BMI, HOMA-IR and HbA1c					
3.42.	Safety	SAFE_T17	Summary of Weight (kg) by Visit		All
3.43.	Safety	LB1	Summary of Change from Baseline in Weight (kg) by Visit		All
3.44.	Safety	SAFE_T7	Statistical Analysis of Change from Baseline in Weight (kg) by Visit- MMRM		All

Safety: Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.45.	Safety	SAFE_T18	Summary of Proportion of Subjects with Change from Baseline in Weight (>=3% and >=10%) at Week X		All
3.46.	Safety	SAFE_T17	Summary of BMI (kg/m2) by Visit		All
3.47.	Safety	LB1	Summary of Change from Baseline in BMI (kg/m2) by Visit		All
3.48.	Safety	SAFE_T5	Summary of Changes in BMI (kg/m2) from Baseline to Week X -Shift Table		All
3.49.	Safety	SAFE_T7	Statistical Analysis of Change from Baseline in BMI (kg/m2) by Visit- MMRM		All
3.50.	Safety	SAFE_T17	Summary of HOMA-IR by Visit		All
3.51.	Safety	LB1	Summary of Change from Baseline in HOMA-IR by Visit - Loge Transformed Data		All
3.52.	Safety	SAFE_T7	Statistical Analysis of Change from Baseline in HOMA-IR by Visit- Loge Transformed Data - MMRM		All
3.53.	Safety	SAFE_T19	Statistical Analysis of Variables Associated with ≥2 HOMA-IR at Week X – Logistic Regression		All
3.54.	Safety	SAFE_T19	Statistical Analysis of Variables Associated with ≥3 HOMA-IR at Week X – Logistic Regression		All
3.55.	Safety	SAFE_T19	Statistical Analysis of Variables Associated with ≥4 HOMA-IR at Week X – Logistic Regression		All
3.56.	Safety	SAFE_T17	Summary of HbA1c by Visit		All

Safety: Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.57.	Safety	LB1	Summary of Change from Baseline in HbA1c by Visit		All
3.58.	Safety	SAFE_T7	Statistical Analysis of Change from Baseline in HbA1c by Visit - MMRM		All

Safety: Tables					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Other Safety Analyses					
3.59.	Safety	SAFE_T8	Summary of True Positive Suicidal Indication Alerts Based on eCSSRS by Visit		All
3.60.	Safety	SAFE_T9	Summary of Subjects with eCSSRS Suicidal Ideation or Behaviour at Baseline		All
3.61.	Safety	SAFE_T9	Summary of Subjects with Post Baseline eCSSRS Suicidal Ideation or Behaviour		All
3.62.	Safety	SAFE_T10	Summary of Characteristics of Post Baseline Adverse Events of Special Interest	Present each AESI in a separate table. Table numbering should be from 3.621 to 3.628	All

15.16.9. Safety Figures

Safety: Figures					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
3.1.	Safety	AE10	Plot of Common (>=2%) Adverse Events and Relative Risk		All
Laboratory: Biomarkers					
3.2.	Safety	LIPID7	Heatmap Plot of NCEP Categories in Lipids Over Time		All
3.3.	Safety	SAFE_F2	Line Plot of Adjusted Mean (95% CI) Change from Baseline in Renal Biomarkers Over Time — MMRM		All
3.4.	Safety	SAFE_F3	Line Plot of Ratio of Geometric Means (95% CI) in Renal Biomarkers Over Time - Loge Transformed Data - MMRM		All
3.5.	Safety	SAFE_F2	Line Plot of Adjusted Mean (95% CI) of Change from Baseline in Bone Biomarkers Over Time — MMRM		All
3.6.	Safety	SAFE_F2	Line Plot of Ratio of Geometric Means (95% of CI) in Inflammatory Biomarkers Over Time - Loge Transformed - MMRM		All
3.7.	Safety	SAFE_F5	Line Plot of Adjusted Mean (95% CI) of Change from Baseline in Weight (kg) Over Time — MMRM		All
3.8.	Safety	SAFE_F5	Line Plot of Adjusted Mean (95% CI) of Change from Baseline in BMI (kg/m2) Over Time — MMRM		All

Safety: Figures					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.9.	Safety	SAFE_F2	Line Plot of Ratio of Geometric Means (95% of CI) in HOMA-IR Over Time - Loge Transformed Data – MMRM		All
3.10.	Safety	SAFE_F5	Line Plot of Adjusted Mean (95% CI) of Change from Baseline in HbA1c Over Time — MMRM		All
Other Safety					
3.11.	Safety	LIPID7	Heatmap Plot of BMI (kg/m2) Categories Over Time		All
3.12.	Safety	LIVER9	Scatter Plot of Maximum ALT vs. Maximum Total Bilirubin		All

15.16.10. Virology Tables

Virology: Tables					
No.	**Population**	**GSK Statistical Display Standard/ TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.1.	CVW	VIR_T1	Summary of INI Mutations at Baseline and Time of CVW at or prior to Week X		All
4.2.	CVW	VIR_T2	Summary of Major Mutations of NRTI, NNRTI and PI Classes by region at Baseline and Time of CVW at or prior to Week X		All
4.3.	CVW	VIR_T3	Summary of Genotype at Baseline and Time of CVW by Genotypic Cut-Off at or prior Week X		All
4.4.	CVW	VIR_T4	Summary of Phenotype at Time of CVW by Phenotypic Cut-off at or prior Week X		All
4.5.	CVW	VIR_T5	Summary of Phenotype at time of CVW by Number of Drugs to Which Subject are Resistant at or prior Week X		All
4.6.	CVW	VIR_T6	Summary of Fold Change to DTG, 3TC at - Time of CVW at or prior to Week X		All
4.7.	CVW	VIR_T7	Summary of Subject Accountability: Genotypes Available at or prior to Week X		All
4.8.	CVW	VIR_T8	Summary of Subject Accountability: Phenotypes Available at or prior to Week X		All

15.16.11. Pharmacokinetic Tables

There is no pharmacokinetic analysis planned in this study.

15.16.12. Pharmacokinetic Figures

There is no pharmacokinetic analysis planned in this study.

15.16.13. Health Outcomes Tables

Health Outcomes : Tables					
No.	**Population**	**GSK Statistical Display Standard/ TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Treatment Satisfaction (HIVTSQ)					
6.1.	ITT-E	THO1	Summary of HIVTSQ Individual Item Scores by Visit		All
6.2.	ITT-E	THO2	Summary of HIVTSQ Total Score, Lifestyle/Ease and General Satisfaction/Clinical Sub-score by Visit		All
6.3.	ITT-E	THO2	Summary of Change from Baseline in HIVTSQ Total Score, Lifestyle/Ease and General Satisfaction/Clinical Sub-score by Visit		All
6.4.	ITT-E	THO3	Statistical Analysis of HIVTSQ Total Score, Lifestyle/Ease and General Satisfaction/Clinical Sub-score Change from Baseline - MMRM		All
6.5.	ITT-E	THO3	Statistical Analysis of HIVTSQ Total Score, Lifestyle/Ease and General Satisfaction/Clinical Sub-score Change from Baseline by Subgroups - MMRM		All
Symptom Distress Module					
6.6.	ITT-E	THO4	Summary of SDM Symptom Count by Visit		All

Health Outcomes : Tables					
No.	**Population**	**GSK Statistical Display Standard/ TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.7.	ITT-E	THO4	Summary of SDM Symptom Bother Score by Visit		All
6.8.	ITT-E	THO4	Summary of SDM Symptom Bother Score Change from Baseline by Visit		All
6.9.	ITT-E	THO5	Percentage of Subjects with Each Type of Symptom as per the SDM by Visit		All
6.10.	ITT-E	THO6	Percentage of Subjects in SDM Symptom Bother Score Categories by Visit		All
6.11.	ITT-E	THO3	Statistical Analysis of Change from Baseline in SDM Symptom Bother Score at Week X– MMRM		All
6.12.	ITT-E	THO3	Statistical Analysis of Change from Baseline in SDM Symptom Bother Score by Subgroups at Week X– MMRM		All

Health Outcomes : Tables					
No.	**Population**	**GSK Statistical Display Standard/ TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Willingness to switch					
6.13.	ITT-E	THO8	Summary of Reasons for Willingness to Switch		All

15.16.14. Health Outcomes Figures

Health Outcomes : Figures					
No.	**Population**	**GSK Statistical Display Standard/ TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Treatment Satisfaction (HIVTSQ)					
6.1.	ITT-E	FHO1	Line Plot of Adjusted Mean (95% CI) Change from Baseline in HIVTSQ Total Treatment Satisfaction Score, Lifestyle/Ease and General Satisfaction/Clinical Sub-score Over Time		All
Symptom Distress Module					
6.2.	ITT-E	FHO1	Line Plot of Adjusted Mean (95% CI) Change from Baseline in SDM Symptom Bother Score Over Time		All

15.16.15. ICH Listings

ICH: Listings					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	ITT-E	ES2	Listing of Reasons for Study Withdrawal	ICH E3	All
2.	ITT-E	SD2	Listing of Reasons for Study Treatment Discontinuation	ICH E3	All
Protocol Deviation					
3.	ITT-E	DV2	Listing of Important Protocol Deviations	ICH E3. Listing to be run regardless of relationship to COVID-19	All
4.	ITT-E	IE4	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	All
Populations Analysed					
5.	ITT-E	SP3a	Listing of Protocol Deviations Leading to Exclusion from the Per Protocol Population	ICH E3	All
6.	ITT-E	DV2	Listing of Protocol Deviations Related to COVID-19	ICH E3 Include a column to flag Important PDs	All

ICH: Listings					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Demographic and Baseline Characteristics					
7.	ITT-E	DM2	Listing of Demographic Characteristics	ICH E3	All
8.	ITT-E	DM10	Listing of Race	ICH E3	All
Efficacy					
9.	ITT-E	EFF_L1	Listing of Study Outcome (≥ / < 50 c/mL) at Week 48 – Snapshot Analysis		All
10.	ITT-E	EFF_L2	Listing of Quantitative and Qualitative Plasma HIV-1 RNA Data		All
11.	ITT-E	EFF_L1	Listing of Study Outcome (≥ / < 50 c/mL) at Week 48 – Modified Snapshot Analysis		All
Exposure and Treatment Compliance					
12.	Safety	EX3	Listing of Exposure Data	ICH E3	All
Adverse Events					
13.	Safety	AE8	Listing of All Adverse Events	ICH E3	All
14.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	All
15.	Safety	AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	All

ICH: Listings					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
16.	Safety	PSRAE1	Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Section 1- Section 2)	ICH E3	All
17.	Safety	PSRAE3	Listing of Possible Suicidality-Related Adverse Event Data: Possible Cause(s) (Section 3)		All
18.	Safety	PSRAE4	Listing of Possible Suicidality-Related Adverse Event Data (Section 4)		All
19.	Safety	PSRAE5	Listing of Possible Suicidality-Related Adverse Event Data (Section 5- Section 8)		All
All Laboratory					
20.	Safety	LB5	Listing of All Laboratory Data for Subjects with Any Value of Potential Clinical Importance	Include Chemistry, Hematology and Lipids. ICH E3	All
21.	Safety	LB5	Listing of Urinalysis Data for Subjects with Any Value of Potential Clinical Importance		All

ICH: Listings					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Vital Signs					
22.	Safety	VS4	Listing of Vital Signs	ICH E3	All

15.16.16. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population					
23.	Screened	ES7	Listing of Reasons for Screen Failure	Journal Guidelines GSK Statistical Display Standard	All
24.	ITT	TA1	Listing of Planned Randomized and Actual Strata and Treatment Assignments		All
25.	ITT	POP_L1	Listing of Subjects Randomized but not Treated		All
26.	Screened	POP_L2	Listing of Subjects Enrolled by Country and Site ID		All

Non-ICH: Listings					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
27.	Screened	ES9	Listing of Subjects Who Were Rescreened		All
28.	ITT-E	POP_L3	Listing of Visit Dates		All
29.	Screened	POP_L4	Listing of Study Populations		All
30.	ITT-E	BASELINE6	Listing of Hepatitis Test Results at Entry		All
31.	ITT-E	CDC3	Listing of CDC Classification of HIV Infection at Baseline		All
32.	ITT-E	RF2	Listing of HIV Risk Factors		All
33.	ITT-E	BASELINE7	Listing of Screening Cardiovascular Risk Assessment Data		All
34.	ITT-E	MH2	Listing of Current and Past Medical Conditions at Baseline		All
35.	ITT-E	POP_L7	Listing of Relationship Between Concomitant ATC Level 1, Ingredient and Verbatim Text		All
36.	ITT-E	CM2	Listing of Concomitant Medications	GSK Statistical Display Standard	All
37.	ITT-E	CM2	Listing of Antiretroviral Therapy Stopped Prior to Screening		All
38.	ITT-E	CM2	Listing of Antiretroviral Therapy Received at Screening		All

Non-ICH: Listings					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
39.	ITT-E	CM2	Listing of On-Treatment Antiretroviral Therapy Starting after Day 1		All
40.	ITT-E	CM2	Listing of Antiretroviral Therapy Starting after Treatment Discontinuation		All
41.	ITT-E	POP_L8	Listing of Relationship Between Concomitant ATC Level 4, Ingredient and Verbatim Text		All
42.	ITT-E	POP_L12	Listing of Menopause History		All
Efficacy					
43.	ITT-E	VF4	Listing of Plasma HIV-1 RNA data and CD4+ cell count data for subjects with Confirmed Virologic Withdrawal		All
44.	ITT-E	EFF_L4	Listing of CD4+ Cell Count Data		All
45.	ITT-E	EFF_L5	Listing of CD8+ and CD4+/CD8+ Cell Count Ratio Data		All
46.	ITT-E	HIV4	Listing of Stage 3 HIV-1 Associated Conditions		All
47.	ITT-E	EFF_L6	Listing of Subjects Treatment-related discontinuation = Failure (TRDF)		All
48.	ITT-E	EFF_L6	Listing of Subjects Efficacy-related discontinuation = Failure (ERDF)		All

Non-ICH: Listings					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Safety					
49.	Safety	EG3	Listing of ECG Findings		All
50.	Safety	SAFE_L1	Listing of Post Baseline Maximum ALT and Maximum Bilirubin		All
51.	Safety	SAFE_L2	Listing of Subjects Meeting Hepatobiliary Abnormality Criteria – All Post-Baseline Abnormalities		All
52.	Safety	SAFE_L3	Listing of eCSSRS Suicidal Ideation and Behaviour Data Alerts (4-9)		All
53.	Safety	SAFE_L4	Listing of eCSSRS Suicidal Ideation and Behaviour Data		All
54.	Safety	SAFE_L5	Listing of eCSSRS False Positive Alerts with Corresponding Reasons		All
55.	Safety	SAFE_L5	Listing of all eCSSRS True Positives, with Corresponding Reasons and AE or SAE status		All
56.	Safety	SAFE_L6	Listing of Subjects Who Became Pregnant During the Study		All
57.	Safety	SAFE_L7	Patient Profiles for Subjects Meeting Protocol Defined Liver Stopping Criteria		All
58.	Safety	SAFE_L7	Patient Profiles for Subjects Meeting Confirmed Virologic Withdrawal Criteria		All

Non-ICH: Listings					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
59.	Safety	SAFE_L7	Patient Profiles for Subject Excluded from Safety Population Due to Non-Study Treatment Ongoing at Randomisation		All
60.	Safety	SAFE_L8	Listing of Cardiovascular Events		All
61.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events		All
62.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text		All
63.	Safety	LB14	Listing of Laboratory Data with Character Results		All
64.	Safety	PAN12	Listing of Subjects with an Adverse Event of Suspected, Probable, Confirmed for COVID-19 Infection		All
65.				Covered in 64	
Hepatobiliary (Liver)					
66.	Safety	MH2	Listing of Medical Conditions for Subjects with Liver Stopping Events		All
67.	Safety	SU2	Listing of Substance Use for Subjects with Liver Stopping Events		All
68.	Safety	PK07	Listing of Plasma DTG Pharmacokinetic for Subjects with Liver Stopping Events		All
Virology					
69.	CVW	VIR_L1	Listing of All Genotypic Data – CVWs		All

Non-ICH: Listings					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
70.	pPVW	VIR_L1	Listing of All Genotypic Data – pPVWs		All
71.	CVW	VIR_L2	Listing of Genotype by Genotypic Cut-Off – CVWs		All
72.	pPVW	VIR_L2	Listing of Genotype by Genotypic Cut-Off – pPVWs		All
73.	CVW	VIR_L3	Listing of All Phenotypic Data – CVWs		All
74.	pPVW	VIR_L3	Listing of All Phenotypic Data – pPVWs		All
75.	CVW	VIR_L4	Listing of Replication Capacity – CVWs		All
76.	pPVW	VIR_L4	Listing of Replication Capacity – pPVWs		All
77.	CVW	VIR_L5	Listing of Net Assessment Score – CVWs		All
78.	pPVW	VIR_L5	Listing of Net Assessment Score – pPVWs		All
79.	CVW	VIR_L7	Listing of Genotypic and Phenotypic Data for Subjects with Confirmed Virologic Withdrawal Criteria		All
80.	pPVW	VIR_L7	Listing of Genotypic and Phenotypic Data for Subjects with Potential Precautionary Virologic Withdrawal Criteria		All

Non-ICH: Listings					
No.	**Population**	**GSK Statistical Display Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
80.1	ITT-E	VIR_L7	Listing of Genotypic and Phenotypic Data for Subjects Last on Study HIV-1 RNA >400 c/mL with Resistance Testing		Week 48
81.	pPVW	VF4	Listing of Plasma HIV-1 RNA data and CD4+ cell count data for subjects with Potential Precautionary Virologic Withdrawal Criteria		All
Health Outcomes					
82.	ITT-E	LHO1	Listing of HIV Treatment Satisfaction Questionnaire Scores (HIVTSQ)		All
83.	ITT-E	LHO2	Listing of Symptom Distress Module Outcome		All
84.	ITT-E	LHO3	Listing of Willingness to Switch		All
Impact of COVID-19 Pandemic					
85.	ITT-E	PAN7	Listing of All Subjects with Visits and Assessments Impacted by COVID-19 Pandemic		
86.	Screened	PAN5	Listing of Country Level Start Dates of COVID-19 Pandemic Measures		

15.17. Appendix 17: Example Mock Shells for Data Displays

Available Upon Request.