Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)

Title	:	Reporting and Analysis Plan for study 205861: An open-label, single arm study to evaluate the week 48 efficacy and safety of a two-drug regimen of dolutegravir/lamivudine (DTG/3TC) as a fixed dose combination (FDC), in antiretroviral therapy (ART)-naive HIV-1-infected adolescents, ≥12 to <18 years of age who weigh at least 25 kg.
Compound Number	:	GSK1349572 + GR109714 (GSK3515864)
Effective Date	:	14-JAN-2022

Description :

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 205861/Amendment 03.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverables for IDMC, Week 48, Week 96 and Week 144.
- The IDMC outputs will be a subset of outputs detailed in this RAP document and as per analysis described within this RAP document. The IDMC charter documents the outputs required.
- This version of the RAP is amendment 1 to the originally approved RAP dated 12-FEB-2019.

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The main changes included in RAP Amendment 1 are as follows:

- Addition of COVID-19 assessments following emergence of COVID-19 pandemic.
- Addition of sensitivity assessments due to a fraud issue at site PPD
- A planned retrospective, exploratory Bayesian analysis added.
- General changes have also been made to be in-line with the study team expectations, improve consistency with the protocol and include new standards.

The following outputs have been added:

Output	Output Title
Table 1.3	Summary of Screening Status and Reasons for Screen Failure
Table 1.4	Summary of Number of Subjects Attending Nominal and Actual Analysis Visits
Table 1.5	Summary of Recruitment by Country and Site Before & After Implementation of Pandemic Measures
Table 1.6	Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Study Conclusion Record
Table 1.9	Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Continuation Phase Conclusion Record
Table 1.10	Summary of Reasons for Withdrawal by Visit
Table 1.11	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment by Relationship to COVID-19 Pandemic
Table 1.28	Sensitivity Analyses 1: Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Study Conclusion Record
Table 1.29	Sensitivity Analyses 2: Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Study Conclusion Record
Table 1.30	Sensitivity Analyses 1: Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Treatment Phase Conclusion Record
Table 1.31	Sensitivity Analyses 2: Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Treatment Phase Conclusion Record
Table 1.32	Sensitivity Analyses 1: Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Extension Phase Conclusion Record
Table 1.33	Sensitivity Analyses 2: Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Extension Phase Conclusion Record
Table 1.36	Sensitivity Analyses 1: Summary of Demographic Characteristics
Table 1.37	Sensitivity Analyses 2: Summary of Demographic Characteristics

Table 3.46	Sensitivity Analyses 2: Summary of Adverse Events Leading to Withdrawal from Study/Permanent Discontinuation of Study Treatment
Figure 3.3	Line Plot of Median (IQR) Serum Creatinine & eGFR Over Time
Listing 53	Listing of COVID-19 Assessments and Symptom Assessments for Subjects with COVID-19 Adverse Events
Listing 56	Listing of Genotypic Data and Treatment Emergent Genotypic Mutations - Confirmed Virological Withdrawal Subjects

The following outputs have been removed:

Output	**Output Title**
Table 1.5	Summary of Subject Accountability: Withdrawals from Study Treatment/Investigational Product by Visit
Table 1.8	Summary of Subjects with Inclusion/Exclusion Criteria Deviations
Table 1.10	Summary of Race and Racial Combinations
Table 1.24	Summary of Concomitant ART Medication Ingredient Combinations
Listing 33	Listing of Subjects Who Were Rescreened
Listing 34	Listing of Visit Dates
Listing 40	Listing of History of Cardiac Therapeutic Procedures
Listing 43	Listing of Relationship Between ATC Level 1, Ingredient and Verbatim Text
Listing 46	Listing of Relationship Between ATC Level 4, Combination, and Verbatim Text for ART
Table 2.6	Summary of Proportion of Subjects with Observed Plasma HIV-1 RNA < 50 c/mL by Visit
Table 2.10	Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Withdrawal at Week 48 - Treatment Related Discontinuation = Failure
Table 2.13	Summary of Post-Baseline HIV-1 Associated Conditions Including Recurrences

Listing 30	Listing of Deaths
Listing 51	Listing of Cardiovascular Events
Listing 55	Listing of Liver Monitoring/Stopping Event Reporting
Listing 56	Listing of Liver Event Information for RUCAM Score
Listing 57	Listing of Liver Biopsy Details
Listing 58	Listing of Liver Imaging Details
Listing 59	Listing of Past and Current Liver Disease Medical Conditions
Listing 60	Listing of Laboratory Data from Liver Event Follow-Up
Listing 68	Patient profiles for subjects meeting protocol defined liver stopping criteria
Listing 70	Listing of Liver Event Results and Time of Event Relative to Treatment
Listing 73	Listing of Treatment Emergent Genotypic Mutations
Listing 74	Listing of Phenotype and Phenotypic Cut-Off – CVWs
Table 5.9	Mean (+/-SD) DTG Pre-dose Concentration versus Visit Plot
Table 5.10	Mean (+/-SD) 3TC Pre-dose Concentration versus Visit Plot
Table 5.11	Median (range) DTG Pre-dose Concentration versus Visit Plot
Table 5.12	Median (range) 3TC Pre-dose Concentration versus Visit Plot

The following outputs have been modified (Note: the output numbers may have changed in Amendment 1 and the below modifications describe only changes to titles and exclude descriptions of changes to shell bodies, footnotes etc.) :

- Table 1.3 (Summary of Subject Disposition: Treatment Phase Conclusion Record) title updated to reflect the inclusion of subject status and to display the number of subjects (along with reasons) for withdrawal based on the relationship to COVID-19.
- Table 1.4 (Summary of Subject Accountability: Extension Phase Conclusion Record) title updated to reflect the inclusion of subject status and be consistent in the use of 'disposition' for similar outputs i.e. Table 1.3 immediately above. Output also updated to display the number of subjects (along with reasons) for withdrawal based on the relationship to COVID-19.

- Table 1.6 (Summary of Important Protocol Deviations) updated to display deviations based on the relationship to COVID-19.
- Listing 44 (Listing of Prior Antiretroviral Therapy) updated to display therapy stopped before Screening.
- Table 2.1 (Summary of Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 – Snapshot Analysis) title updated to reflect the inclusion of Week 24 Snapshot Analysis based on the Intent-To-Treat Exposed (ITT-E) population.
- Table 2.3 (Summary of Study Outcomes (<50 c/mL) at Week 48 – Snapshot Analysis) title updated to reflect the inclusion of Week 24 Snapshot Analysis based on the ITT-E population.
- Table 2.7 (Summary of Proportion of Subjects with Observed Plasma HIV-1 RNA < 200 c/mL by Visit) title updated to remove 'Observed' and add '- Snapshot Analysis' to ensure consistency with similar outputs.
- Table 2.8 (Proportion of Subjects Meeting Confirmed Virologic Withdrawal Criteria by Visit) title updated to add 'Cumulative' at the beginning.
- Figure 2.3 (Individual Plasma HIV-1 RNA and CD4+ Profiles by Visit for subjects with at least one SVW visit) title updated to replace 'SVW' with 'CVW'.
- Figure 2.4 (Individual CD8+ and Ratio Profiles by Visit for subjects with at least one SVW visit) title updated to replace 'SVW' with 'CVW'.
- Listing 48 (Listing of HIV-1 Associated Conditions) title updated to add 'Stage 3' to reflect only subjects with HIV-1 infection stage 3 are included.
- Table 3.1 (Summary of Extent of Exposure to Investigational Product – Treatment and Extension Phases) updated to not limit this output to specific study phases therefore, '-Treatment and Extension Phases' removed from the title.
- Table 3.2 (Summary of All Adverse Events by System Organ Class) title updated to add 'Preferred Term' to improve the accuracy of the output contents.
- Table 3.6 (Summary of Drug-Related Toxicity Grade 2-5 Adverse Events) title updated to add 'by Frequency' to improve the accuracy of the output contents.
- Table 3.11 (Summary of Non-Serious Adverse Events by Preferred Term with Occurrences >=5%) title updated to add 'Common', 'System Organ Class' and 'Number of Subjects' to improve the accuracy of the output contents.
- Table 3.14 (Summary of Drug-Related Serious Adverse Events by System Organ Class) title updates to add 'Preferred Term' to improve the accuracy of the output contents.
- Table 3.21 (Summary of Chemistry Changes from Baseline by Visit) title updated to add 'at or prior to Week X' to reflect the contents of this output will be presented at or prior to the visit of the relative analysis timepoint e.g. Week 48.

- Table 3.23 (Summary of Hematology Changes from Baseline by Visit) title updated to add ‘at or prior to Week X’ to reflect the contents of this output will be presented at or prior to the visit of the relative analysis timepoint e.g. Week 48.
- Table 3.29 (Summary of Positive Suicidal Indication Alerts Based on eCSSRS by Visit) title updated to add ‘True’ to indicate only true positive suicidal indication alerts are included in this output.
- Table 3.32 (Summary of Tanner Staging Score) title updated to add ‘at or prior to Week X’ to reflect the contents of this output will be presented at or prior to the visit of the relative analysis timepoint e.g. Week 48. Title also update to add ‘by Visit’ to indicate contents will be presented on a by visit basis.
- Table 3.33 (Summary of Tanner Staging Score Changes from Baseline) title updated to add ‘at or prior to Week X’ to reflect the contents of this output will be presented at or prior to the visit of the relative analysis timepoint e.g. Week 48. Title also update to add ‘by Visit’ to indicate contents will be presented on a by visit basis.
- Listing 52 (Listing of All ECG Findings for Subjects with an Abnormal Finding) title updated to remove ‘All’ and ‘Subjects with an Abnormal Finding‘ to reflect the contents of the output will not be limited to only data with abnormal findings.
- Listing 53 (Listing of Vital Signs) title updated to include ‘– Including Height, Weight and BMI’ to reflect Height, Weight and BMI are included in the contents of this output now.
- Table 4.3 (Summary of IN Mutations for Subjects Meeting Confirmed Virologic Withdrawal Criteria) title updated to add ‘at or prior to Week X’ to reflect the contents of this output will be presented at or prior to the visit of the relative analysis timepoint e.g. Week 48.
- Table 4.4 (Summary of Treatment-Emergent IN Mutations for Subjects Meeting Confirmed Virologic Withdrawal Criteria) title updated to add ‘at or prior to Week X’ to reflect the contents of this output will be presented at or prior to the visit of the relative analysis timepoint e.g. Week 48.
- Table 4.5 (Summary of Genotypic Data of NRTI, NNRTI, and PI Classes for Subjects Meeting Confirmed Virologic Withdrawal Criteria) title updated to add ‘at or prior to Week X’ to reflect the contents of this output will be presented at or prior to the visit of the relative analysis timepoint e.g. Week 48.
- Table 4.7 (Summary of Phenotype for Subjects Meeting Confirmed Virologic Withdrawal Criteria by Phenotypic Cut-off) title updated to add ‘at or prior to Week X’ to reflect the contents of this output will be presented at or prior to the visit of the relative analysis timepoint e.g. Week 48. Title also updated to add ‘at Time of CVW’.
- Figure 5.1 (Individual DTG Plasma Concentration–Time Plot) title updated to add ‘-Intensive Sampling’ to indicate the figure is presented based on the Intensive Pharmacokinetic Population.

- Figure 5.2 (Individual 3TC Plasma Concentration–Time Plot) title updated to add '- Intensive Sampling' to indicate the figure is presented based on the Intensive Pharmacokinetic Population.
- Figure 5.7 (Individual DTG Pre-dose Concentration versus Visit Plot) title updated to add '- Sparse Sampling' to indicate the figure is presented based on the sparse subjects with the Sparse + Trough Pharmacokinetic Population. Title also updated to add 'Scatter Plot of'.
- Figure 5.8 (Individual 3TC Pre-dose Concentration versus Visit Plot) title updated to add '- Sparse Sampling' to indicate the figure is presented based on the sparse subjects with the Sparse + Trough Pharmacokinetic Population. Title also updated to add 'Scatter Plot of'.

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1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	• The purpose of this reporting and analysis plan (RAP) is to provide details of planned analyses and data displays for reporting results of study 205861 DANCE. These analyses may be included in regulatory submissions, study reports, publications and pricing and reimbursement dossiers.
Protocol	• This RAP is based on the protocol amendment 03 [(Dated: 20/NOV/2020) and the original protocol (Dated:04/APR/2018) of study 205861 DANCE (GSK Document No.: 2017N326062_00 and GSK Document No.: 2017N326062_03).
Primary Objective	• To assess the antiviral activity of Dolutegravir (DTG)/ Lamivudine (3TC) in antiretroviral naïve HIV-1 infected adolescents.
Primary Endpoint	• The proportion of participants with plasma HIV-1 Ribonucleic acid (RNA) less than 50 c/mL at Week 48 using the Snapshot algorithm (ITT-E population).

Study Design	• This is a Phase IIIb, single-arm, open-label, multi-center assessment of DTG/3TC in approximately 30 HIV-1 infected, treatment-naive adolescents with plasma HIV-1 RNA between 1,000 and ≤500,000 c/mL. All enrolled participants will receive an open-label, two-drug regimen of DTG/3TC for 48 weeks. Participants who successfully complete 48 weeks of treatment may enter the study Extension Phase for an additional 96 weeks. At the end of the study, participants who continue to receive benefit from DTG/3TC and for whom these medications are not locally accessible, will have access to medication in a Continuation Phase until it is available locally (See Protocol Section 7.10).
	• Data from this study will be used to assess the safety, efficacy and tolerability of this combination of DTG/3TC in adolescents relative to what is observed in large and controlled clinical studies being conducted in adults.
	• The study will comprise:
	  • Screening Phase (approximately Day -28 to Day 1)
	  • Treatment Phase (Day 1 to Week 48)
	  • Extension Phase (Week 48 to Week 144)
	  • Continuation Phase (Week 144+).

Planned Analyses	• The Primary Analysis at Week 48 will be conducted when all subjects complete their 48 Week visit. For patients that are not continuing into the Extension phase and conclude at the end of the treatment phase, a follow-up/final visit will be scheduled 4 weeks after the Week 48 visit and all visits up to and including the follow up/final visit will be included in the Week 48

Overview	Key Elements of the RAP
	Analysis. Secondary analyses relating to Week 24 data will also be performed at this time. • Secondary analyses will be conducted at Week 96 and Week 144. • No external presentation or publication will occur until at least all subjects have completed the Week 48 visit (primary endpoint visit). • An ad-hoc review of data by the Independent Data Monitoring Committee (IDMC) will be triggered if the number of Confirmed Virologic Withdrawals (CVW) exceeds thresholds pre-specified in the IDMC charter. • A final analysis will be performed at the end of the continuation phase after the last subject leaves the study (study conclusion). • Further data cuts and analysis may be conducted as necessary to support regulatory submissions and publications. • In the event of early termination of the study a full analysis will be implemented.
Analysis Populations	• All Screened Subjects • Safety • Safety Sensitivity Population 1 (Safety Sens 1) • Safety Sensitivity Population 2 (Safety Sens 2) • Intent-To-Treat Exposed (ITT-E) • Intent-to-Treat Exposed – Extension Phase (ITT-E EP) • Intent-to-Treat Exposed Sensitivity Population 1 (ITT-E Sens 1) • Intent-to-Treat Exposed Sensitivity Population 2 (ITT-E Sens 2) • Intent-to-Treat Exposed – Extension Phase Sensitivity Population 1 (ITT-E EP Sens 1) • Intent-to-Treat Exposed – Extension Phase Sensitivity Population 2 (ITT-E EP Sens 2) • Per-Protocol (PP) • Confirmed Virologic Withdrawal (CVW) • Pharmacokinetic • Sparse + Trough Pharmacokinetic Population • Intensive Pharmacokinetic Population
Primary Analyses	• The primary endpoint of the proportions of subjects meeting the criteria of plasma HIV 1 RNA <50 copies/mL (c/mL) as defined by the Snapshot

Overview	Key Elements of the RAP
	algorithm will be reported with exact Clopper Pearson 95% confidence intervals at Week 48.
Secondary Analyses	• Secondary analyses will be conducted for additional efficacy, safety, PK, and virologic endpoints.
Supportive, Sensitivity and Exploratory Analyses	• Efficacy related analysis described above will also be performed using the PP population and the results will be compared for consistency with those from the ITT-E population. • Efficacy related analysis described above will also be performed using the ITT-E Sens 1 and ITT-E Sens 2 populations to assess the impact after removal of data from one site in Kenya which was closed following sponsor investigation of significant quality issues to provide more reliable estimates for snapshot analyses (see Section 3.4). The results will be compared with the results from the ITT-E and PP populations. • Safety related analysis described above will also be performed using the Safety Sens 1 and Safety Sens 2 populations to assess the impact after removal of data from one site in Kenya which was closed following sponsor investigation of significant quality issues (see Section 3.4). The results will be compared with the results from the Safety population. • An exploratory, retrospective Bayesian dynamic borrowing analysis will be performed to investigate the posterior outcomes for a range of prior weights on previous adult study results. Planned analysis will be detailed in a separate document,

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

A few changes were made to the agreed upon sections in the protocol Amendment 3 [(Dated: 20/NOV/2020)]. A summary of these changes are noted below.

Section # and Name	Description of Change and Rationale
Protocol Section 10.3.2: Safety Analyses • The proportion of participants experiencing changes from Baseline in their National Cholesterol Education Program (NCEP) lipid categories will be summarized	• The analysis presenting shift in NCEP lipid categories will not be presented due to small number of patients in the study. Summary of toxicity grades for lipids will be presented and any subject with a treatment emergent toxicity will be looked at on an individual basis.
Protocol Section 10.3.1: Efficacy Analyses	• Sensitivity analyses have been added to present selected outputs that exclude data from a site closed following sponsor investigation of significant quality issues. • An exploratory, retrospective Bayesian dynamic borrowing analysis will be performed to investigate the posterior outcomes for a range of prior weights on previous adult study results.

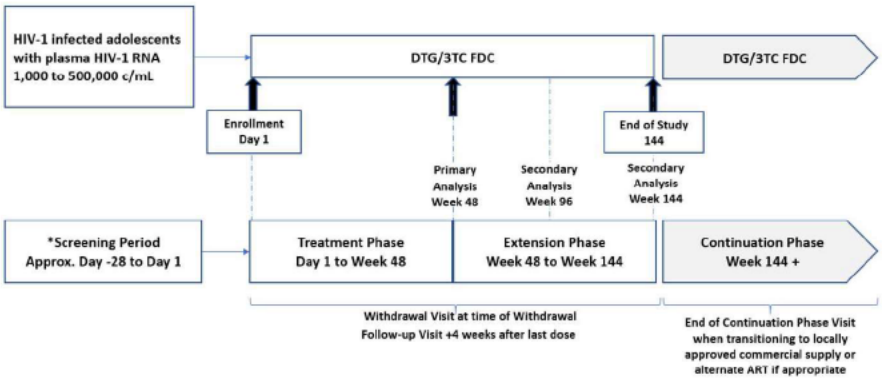
2.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To assess the antiviral activity of DTG/3TC in antiretroviral naïve HIV-1 infected adolescents.	• The proportion of participants with plasma HIV-1 RNA less than 50 c/mL at Week 48 using the Snapshot algorithm (ITT-E population).
Secondary Objectives	**Secondary Endpoints**
• To assess the early antiviral activity of DTG/3TC and to determine the extended long term (≥48 weeks) safety, tolerability, and viral response of DTG/3TC in antiretroviral naïve HIV-1 infected adolescents.	• Proportion of participants with plasma HIV-1 RNA <200 and <50 c/mL at Week 24, Week 96 and Week 144. • Proportion of participants with plasma HIV-1 RNA <200 c/mL at Week 48. • Incidence and severity of AEs and laboratory abnormalities through 144 weeks. • Proportion of participants who discontinue treatment due to AEs through 144 weeks.

Objectives	Endpoints
	• Safety and tolerability assessments at Weeks 96 and 144. • Viral load monitoring after Week 48 through Week 144.
• To evaluate the effect of DTG/3TC on immunologic response from baseline to 24 and 48 weeks	• Change from baseline in CD4+ and CD8+ cell count and ratio at Week 24 and 48. • Incidence of disease progression (HIV associated conditions, AIDS, and death) through Weeks 24 and 48.
• To assess the safety and tolerability of DTG/3TC in HIV-1 infected adolescents at 24 and 48 weeks	• Incidence and severity of AEs and laboratory abnormalities through 24 and 48 weeks. • Proportion of participants who discontinue treatment due to AEs through 24 and 48 weeks.
• To assess DTG and 3TC exposure and to evaluate the steady-state pharmacokinetics of DTG and 3TC in HIV-1 infected adolescents	• Steady-state plasma Pharmacokinetic (PK) parameters of DTG and 3TC will be assessed using intensive PK collected in a subset of participants.
• To assess development of viral resistance to DTG and 3TC in participants experiencing protocol-defined Virologic failure (i.e. meeting confirmed virologic withdrawal criteria).	• Incidence of observed genotypic and phenotypic resistance to DTG and 3TC for participants meeting confirmed virologic withdrawal criteria.

2.3. Study Design

Overview of Study Design and Key Features



* Retesting of an exclusionary lab result (except for exclusionary HIV-1 resistance), is allowed during the screening window (does not require re-screening). In cases of central laboratory assay failure or shipment failure, the screening period may be extended to 35 days to accommodate sample analysis and reporting. Approval of the Medical Monitor is required.

Design Features	• This study will comprise of a Screening Phase (approximately Day -28 to Day 1), a Treatment Phase (Day 1 to Week 48), an Extension Phase (Week 48 to Week 144) and a Continuation Phase (Week 144+).
Participants	• Approximately 80 participants will be screened to achieve 30 enrolled participants and participants who prematurely discontinue the study will not be replaced. • A subset of approximately 12 participants will provide intensive PK samples to ensure data is available from at least 10 evaluable participants.
Dosing	• All participants will receive the fixed dose combination of DTG/3TC (50/300 mg) for once daily dosing. After a Screening Period, all participants will be treated for 48-week Treatment Phase. Participants who successfully complete 48 weeks of therapy and who continue to receive benefit from this two-drug regimen may enter a 96-week study Extension Phase. Participants who successfully complete the Extension Phase and who continue to receive benefit from this two-drug regimen will have access to this regimen in the Continuation Phase until it is approved and available locally.
Treatment Assignment	• This is a Phase IIIb, single-arm, open-label, multi-center assessment of DTG/3TC FDC

2.4. Statistical Hypotheses

This study is designed to assess the antiviral activity of DTG/3TC FDC in antiretroviral naïve HIV-1 infected adolescents at Week 48. Data from this trial is intended to supplement the dataset in adults with data in adolescents. As such, data from this trial will provide 'bridging' information for regulatory authorities and treating clinicians. No formal statistical hypothesis testing will be performed.

3. PLANNED ANALYSES

3.1. IDMC Interim Analyses

An Independent Data Monitoring Committee (IDMC) will be instituted to ensure external objective medical and/or statistical review of efficacy and safety in order to protect the ethical interests and well-being of subjects and to protect the scientific validity of study 205861. Data looks will occur approximately once every 6 months. An ad-hoc review of data by the IDMC will be triggered if the number of Confirmed Virologic Withdrawals (CVW) exceeds thresholds pre-specified in the IDMC charter. Full details of the methods, timing and decision criteria will be pre-specified in the IDMC Charter. A subset of the Primary Analysis outputs will be created for the IDMC analysis and these are noted in Appendix 14.12.

3.2. Primary Analyses

The primary analysis at Week 48 will be conducted when all subjects complete their Week 48 visit. For patients that are not continuing into the Extension phase and conclude at the end of the treatment phase, a follow-up/final visit will be scheduled 4 weeks after the Week 48 visit and all visits up to and including the follow up/final visit will be included in the Week 48 Analysis. If any patient agrees to enter the Extension phase at Week 48 and then decides to withdraw from the study within the 4 week window, the patient will still be counted as entering Extension phase at Week 48 and will be counted as discontinued at final study analysis. Further data cuts and analyses may be conducted as necessary in order to support regulatory submissions and publications.

No external presentation or publication will occur until at least all subjects have completed the Week 48 visit (primary endpoint visit) or the study is stopped early by the IDMC. In event of early study termination, a full analysis will be performed.

3.3. Final Analyses

The primary analysis is at Week 48, this should incorporate all secondary Week 24 analyses. Additional analyses will be performed at Week 96, Week 144 and the end of the continuation phase after last subject leaves the study (study conclusion).

The planned analyses at Weeks 48, 96, and 144 and end of continuation phase will be performed after the completion of the following sequential steps:

- Last subject has completed the relevant visit at Week 48 (96, 144 or end of continuation) as defined in the protocol, including any re-test if required.
- All required database cleaning activities have been completed as specified in the monitoring plan and Data Validation Manual and final database release and database freeze has been declared by Data Management.

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

3.4. Sensitivity Analyses due to Fraud at Study Site

During the conduct of the study, site PPD was closed due to fraud involving the manipulation of Maseno University Ethics Review Committee (MUERC) export permit applications and license approval documents that were required for the shipment of samples to the central laboratory. Source data verification (SDV) was fully completed by PPD for all participants, as well as remote evaluation of data by PPD, ViiV and GSK. Although this investigation did not find evidence of impacts to the data integrity of the clinical database, a subset of the study displays will be presented for sensitivity populations based on two sensitivity population approaches.

One approach will exclude those participants with an absence of Week 48 data as a result of the site closure (Sensitivity Population 1). This approach will provide snapshot-based estimates that more reliably reflect efficacy than the primary approach since these estimates will not be adversely impacted by site closure, an event unrelated to study drug. The other sensitivity analysis will exclude all participants from this site to more generally assess the impact of this site on study outcomes (Sensitivity Population 2).

Displays presented for these populations will be:

Display Section	Display Type	Display Title
Study Populations	Table	Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Study Conclusion Record
Study Populations	Table	Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Treatment Phase Conclusion Record
Study Populations	Table	Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Extension Phase Conclusion Record
Study Populations	Table	Summary of Demographic Characteristics

Display Section	Display Type	Display Title
Study Populations	Table	Distribution of Quantitative Plasma HIV-1 RNA (c/mL) Results at Screening and Baseline
Study Populations	Table	Distribution of CD4+ Cell Count (cells/mm^3) Results at Screening and Baseline
Efficacy	Table	Summary of Study Outcomes (<50 c/mL) at Week 48 – Snapshot Analysis
Efficacy	Table	Summary of Study Outcomes (<200 c/mL) – Snapshot Analysis
Efficacy	Table	Summary of Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL by Visit – Snapshot Analysis
Efficacy	Table	Summary of Proportion of Subjects with Plasma HIV-1 RNA < 200 c/mL by Visit –Snapshot Analysis
Efficacy	Table	Summary of Change from Baseline in CD4+, CD8+ Cell Count and Ratio (cells/mm^3) by Visit
Efficacy	Figure	Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL by Visit
Efficacy	Figure	Proportion (95% CI) of Subjects with HIV-1 RNA <200 c/mL by Visit
Efficacy	Figure	Unadjusted Mean (95% CI) Change From Baseline in CD4+ Cell Count (cells/mm^3) by Visit
Safety	Table	Summary of Extent of Exposure to Investigational Product
Safety	Table	Summary of All Adverse Events by Maximum Toxicity
Safety	Table	Summary of Drug-Related Adverse Events by Maximum Toxicity
Safety	Table	Summary of Serious Adverse Events by System Organ Class and Preferred Term
Safety	Table	Summary of Adverse Events Leading to Withdrawal from Study/Permanent Discontinuation of Study Treatment

3.5. Exploratory and Supportive Bayesian Dynamic Borrowing

As an exploratory and supportive analysis, a retrospective Bayesian Dynamic Borrowing analysis will be performed for the primary efficacy endpoint which will make use of available adult information from two previous studies to inform the paediatric data being collected in this study. Details of the planned analysis will be documented separately.

4. SAMPLE SIZE CONSIDERATIONS

This study will enroll approximately 30 adolescent participants and is proposed to complement the fully powered non-inferiority evaluation of the DTG/3TC combination performed in adults. Approximately 80 participants will be screened to enable enrolment of 30 participants. The reported Week 48 response rates for DTG+2 Nucleoside reverse transcriptase inhibitors (NRTI) from two GEMINI studies in adults are 88% and 90% (ITT-E, % <50 c/mL by Snapshot algorithm). It is therefore reasonable to conservatively expect a lower response rate of 77% (23/30) or 80% (24/30) in adolescents based on their recognized treatment adherence difficulties.

A single arm study with 30 participants will provide an exact Clopper Pearson 95% CI of 61%-92% for an assumed response rate of 80% (% <50 c/mL by Snapshot algorithm at Week 48) or 58%-90% if the assumed response rate is 77%.

5. ANALYSIS POPULATIONS

5.1. Analysis Populations

Population	Definition / Criteria	Analyses Evaluated
All Screened Subjects	• The All Subjects Screened population will consist of all subjects screened for inclusion in the study.	• All Subjects Screened
Safety	• Comprise of all subjects who receive at least one dose of study treatment.	• Safety
Safety Sensitivity Population 1 (Safety Sens 1)	• Comprise of all subjects in the Safety population with the exception of subjects at site PPD who were withdrawn prior to Week 48 due to site closure.	• Safety (sensitivity analyses)
Safety Sensitivity Population 2 (Safety Sens 2)	• Comprise of all subjects in the Safety population with the exception of subjects at site PPD	Safety (sensitivity analyses)
Intent-To-Treat Exposed (ITT-E)	• Comprise of all enrolled subjects who receive at least one dose of study treatment.	• Efficacy
Intent-To-Treat Exposed– Extension Phase (ITT-E EP)	• Comprise of all enrolled subjects who receive at least one dose of study treatment and enter the Extension Phase of the study.	• Efficacy
Intent-To-Treat Exposed Sensitivity Population 1 (ITT-E Sens 1)	• Comprise of all subjects in the ITT-E population with the exception of subjects at site PPD who were withdrawn prior to Week 48 due to site closure.	• Efficacy (sensitivity analyses)
Intent-To-Treat Exposed Sensitivity Population 2 (ITT-E Sens 2)	• Comprise of all subjects in the ITT-E population with the exception of subjects at site PPD	• Efficacy (sensitivity analyses)
Intent-To-Treat Exposed– Extension Phase Sensitivity Population 1 (ITT-E EP Sens 1)	• Comprise of all subjects in the ITT-E population and enter the Extension Phase of the study with the exception of subjects at site PPD who were withdrawn prior to Week 96 due to site closure.	• Efficacy (sensitivity analyses)
Intent-To-Treat Exposed– Extension Phase Sensitivity	• Comprise of all subjects in the ITT-E population and enter the Extension Phase of the study with the exception of subjects at site PPD	• Efficacy (sensitivity analyses)

Population	Definition / Criteria	Analyses Evaluated
Population 2 (ITT-E EP Sens 2)		
Per-Protocol (PP)	• Comprise of all subjects in the ITT-E population with the exception of subjects with significant protocol violations: consisting of not meeting at least one of the protocol inclusion or exclusion criteria or violations which could affect the assessment of antiviral activity (see Appendix 14.1.1).	• Efficacy
Confirmed Virologic Withdrawal (CVW)	• Comprises all subjects in the ITT-E population who have met the derived CVW criteria (see Appendix 14.6.4).	• Genotypic • Phenotypic • Efficacy
Pharmacokinetic Population	• Subjects in the 'Safety' population for whom a pharmacokinetic sample was obtained and analysed.	• PK
Sparse + Trough Pharmacokinetic Population	• All subjects who received at least 1 dose of DTG/3TC Fixed Dose Combination (FDC) and have evaluable sparse and/or trough samples with drug concentrations reported, where samples are collected according to the sparse and trough sampling schedules (Weeks 4, 8, 12, 16, 24, 36, and 48).	• PK
Intensive Pharmacokinetic Population	• The subset of subjects enrolled into intensive PK sampling, who received at least 1 dose of DTG/3TC Fixed Dose Combination (FDC) and have evaluable drug concentrations reported, where samples are collected according to the intensive sampling schedule (Week 1 only).	• PK

5.2. Protocol Deviations

5.2.1. Protocol Deviations

Term	Definition
Protocol Deviation Rules Document	A document describing protocol 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 Clinical Trial Management System (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.
COVID-19 Protocol Deviations	Important protocol deviations relating to the COVID-19 pandemic will be documented in CTMS with their respective rule number followed by 'COVID-19' before text description. All other COVID-19 related protocol deviations not associated with a rule number will be documented with 'COVID-19' before the text description.

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

Important deviations which result in exclusion from the analysis population (Significant deviations) will also be summarised and listed (see Appendix 14.1.1).

Protocol deviations, including COVID-19 protocol deviations, will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Rules Document [13Aug2020, version 2.0].

- Data will be reviewed prior to freezing of the database with the aim of capturing and categorising all important deviations and deviations which may lead to exclusion from the analysis in the protocol deviations SDTM dataset.
- This dataset will be the basis for the summaries and listings of protocol deviations.

6. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

Table 1 provides an overview of appendices within the RAP for outlining general considerations for data analyses and data handling conventions.

Table 1 Overview of Appendices

Section	Component
Section 14.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
Section 14.2	Appendix 2: Time & Events
Section 14.3	Appendix 3: Assessment Windows
Section 14.4	Appendix 4: Treatment States and Phases
Section 14.5	Appendix 5: Data Display Standards & Handling Conventions
Section 14.6	Appendix 6: Derived and Transformed Data
Section 14.7	Appendix 7: Premature Withdrawals & Handling of Missing Data
Section 14.8	Appendix 8: Snapshot and Modified Snapshot Algorithm Details
Section 14.9	Appendix 9: Abnormalities of Potential Clinical Concern
Section 14.10	Appendix 10: Abbreviations & Trademark
Section 14.11	Appendix 11: List of Data Displays
Section 14.12	Appendix 12: Table of Contents

7. STUDY POPULATION ANALYSES

The study population analyses will be based on the ITT-E population, unless otherwise specified.

When descriptive statistics are used to summarize group characteristics or differences, the following statistics will be included: for categorical variables, the number and percent in each category; for continuous variables, the mean, median, standard deviation, quartiles, and range (minimum, maximum).

Table 2 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 14.11: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated	
	Table	Listing
Subject Disposition		
Subjects by Country and Investigator [1]	Y	Y
Subjects Enrolled by Country and Site ID relative to COVID-19 Pandemic measures	Y	
Subjects Attending Nominal and Actual Analysis Visits	Y	
Country Level Listing of Start Dates of COVID-19 Pandemic Measures		Y
Reasons for Screen Failure [1]	Y	Y
Subject Disposition	Y [2,4]	
Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic	Y [3,4]	
Treatment Status and Reasons for Discontinuation of Study Treatment by relationship to COVID-19 Pandemic	Y	
Reasons for Study Treatment Discontinuation		Y
Reasons for Withdrawals	Y [5]	Y
Populations Analysed		
Study Populations [1]	Y	Y
Protocol deviations		
Important Protocol Deviations by Relationship to COVID-19	Y	Y
Deviations Leading to Exclusion from the Per-Protocol Population	Y	Y
Inclusion/Exclusion Criteria Deviations		Y
Demography and baseline characteristics		

Demographic Characteristics [6]	Y	Y
Race and Racial Combinations [7]	Y	Y
Hepatitis Status at Entry	Y	Y
CDC Classification of HIV infection at Baseline	Y	Y
HIV Risk Factor	Y	Y
Distribution of Quantitative Plasma HIV-1 RNA (c/mL) Results at Screening and Baseline	Y	
Distribution of CD4+ Cell Count	Y	
History of Cardiac Therapeutic Procedures		Y
Cardiovascular Risk Assessment		Y
Medical Conditions, Concomitant Medications & Antiretroviral Therapy		
Medical Conditions (Current and Past) at Day 1	Y	Y
Concomitant Medications (non-ART)	Y[8]	Y [9]
Prior ART Medications		Y [10]
Concomitant ART Medications	Y	Y [10]
Other		
IP Accountability [11]		Y
Current Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, and Nervous System Conditions	Y	
Past Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, and Nervous System Conditions	Y	

NOTES:

- Y = Display Generated

1. All Subjects screened population.
2. Subject Disposition by Treatment Phase only.
3. Subject Disposition by Phase (Overall, Study Conclusion, Treatment phase, Extension Phase, Continuation Phase)
4. Subjects who have not been recorded as either completing or withdrawing from the study in the respective phase will be categorized as "Ongoing at time of the analysis" for summary purposes.
5. Displayed by visit.
6. Age, sex, ethnicity, weight, height, BMI (kg/m^2), child-bearing potential and HIV subtype collected at screening.
7. 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.
8. Three separate tables, summarised by Ingredient ATC Level 1, Ingredient combinations and Combination term ATC Level 1 (EG Includes single-ingredient medications with multi-ingredient medications labelled according to the sum of their ingredients, e.g., "TYLENOL Cold and Flu" would appear as "CHLORPHENAMINE MALEATE + DEXTROMETHORPHAN HYDROBROMIDE + PARACETAMOL + PSEUDOEPHEDRINE HYDROCHLORIDE" under the ATC headings for "Nervous System" and "Respiratory System" (the combination's ATC classifications).)
9. One listing for concomitant non-ART medications.
10. One listing for prior ART stopped prior to screening and one listing for concomitant ART.
11. Dispensation information (dates and number of tablets dispensed and returned)

8. PRIMARY EFFICACY ANALYSES

The primary efficacy analyses will be based on ITT-E population, unless otherwise specified.

8.1. Overview of Planned Efficacy Analyses

Table 3 provides an overview of the planned efficacy analyses, with full details of data displays being presented in Appendix 14.11: List of Data Displays.

Table 3 Overview of Planned Primary Efficacy Analyses

Endpoint	Absolute						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Proportion of Subjects with plasma HIV 1 RNA <50 c/mL at week 48 – Snapshot							
Week 48 (ITT-E population)	Y[1]						Y[2]
Study Outcome [3] based on the Snapshot				Y[1]			Y
By visit	Y[4]				Y[5]		

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', 'Intent-To-Treat Exposed Sensitivity 1' and 'Intent-To-Treat Exposed Sensitivity 2' populations.
2. Listing of Quantitative and Qualitative Plasma HIV-1 RNA Data based on the snapshot algorithm.
3. Study outcomes (i.e. HIV-1 RNA >=50 c/mL, HIV-1 RNA <50 c/mL (response below 50 c/mL) or no virologic data at week x window) based on the snapshot algorithm.
4. Including 95% confidence intervals.
5. Line plots, with 95% confidence intervals, for the proportion of subjects with HIV-1 RNA <50 c/mL at each visit.

8.2. Planned Efficacy Statistical Analyses

Primary Statistical Analyses
Endpoint(s)
• Proportion of subjects with plasma HIV-1 RNA <50 c/mL at Week 48 using the Snapshot algorithm for the ITT-E population
Snapshot Dataset
• The Snapshot algorithm treats all subjects without HIV-1 RNA data at the visit of interest (due to missing data or discontinuation of IP prior to the visit window) as non-responders, as well as subjects who switch their concomitant ART prior to the visit of interest in certain scenarios. Since changes in ART are not permitted in this protocol, all such subjects who change ART will be considered non-responders. • Otherwise, virologic response or virologic non-response will be determined by the last available HIV-1 RNA assessment while the subject is On-treatment within the visit of interest analysis window (see Appendix 14.3). • Full details of the Snapshot algorithm are in Appendix 14.6.4.
Statistical Methodology Specification
• The Snapshot algorithm treats all subjects without HIV-1 RNA data at the visit of interest (due to missing data or discontinuation of IP prior to the visit window) as non-responders. The nature of this missing data will be further classified in Snapshot summaries as either 'HIV-1 RNA >=50 c/mL' or 'No Virologic Data at Week 48'. Subjects who change their ART regimen prior to the visit of interest will be considered HIV-1 RNA >=50 c/mL since changes in ART are not permitted in this protocol. • 'HIV-1 RNA >=50 c/mL' includes subjects who changed any ART; subjects who discontinued study drug or study before Week 48 for lack or loss of efficacy, discontinued for other reason while not < 50 c/mL, and subjects who have HIV-1 RNA ≥ 50 c/mL at the visit of interest. • HIV-1 RNA <50 c/mL includes subjects who have HIV-1 RNA <50 c/mL at the visit of interest. • HIV-1 RNA <50 c/mL or HIV-1 RNA >=50 c/mL will be determined by the last available HIV-1 RNA assessment while the subject is On-treatment within the visit of interest analysis window see Appendix 14.3. Full details of the Snapshot algorithm are in Appendix 14.6.4. • Results will be presented for proportion of subjects with corresponding 95% CI (exact Clopper Pearson method).
Results Presentation
• Study outcomes will be summarized and listed. • Quantitative plasma HIV-1 RNA data will be listed including the interpretation of whether the virus is detected or not ('Detected' or 'Not Detected') by the assay.

Primary Statistical Analyses

- Figures: Line plots, with 95% confidence intervals, for the proportion of subjects < 50 c/mL as per the FDA snapshot at each visit.

Supportive and Sensitivity Statistical Analyses

1. PP population analysis:
   - To assess the impact of major protocol deviations, the primary analysis described above will be performed using the Per-Protocol population and the results will be compared for consistency with the results from the ITT-E population.
2. ITT-E Sens 1 population analysis:
   - To assess the impact after removal of participants with an absence of Week 48 data from one site in Kenya which was closed following sponsor investigation of significant quality issues. These results will be compared with the results from the ITT-E population.
3. ITT-E Sens 2 population analysis:
   - To assess the impact after removal of all participants from one site in Kenya which was closed following sponsor investigation of significant quality issues. These results will be compared with the results from the ITT-E population.
4. Bayesian dynamic borrowing analysis (retrospective 'tipping point' analysis):
   - See Section 3.5 for more details.

9. SECONDARY ANALYSES

The secondary endpoint analyses will be based on the ITT-E population, unless otherwise specified.

9.1. Efficacy Analysis

9.1.1. Overview of Planned Efficacy Analyses

Table 4 provides an overview of the planned secondary endpoint analyses, with full details of data displays being presented in Appendix 14.11: List of Data Displays.

Table 4 Overview of Planned Efficacy Analyses

Endpoints	Stats Analysis			Absolute				Change from Baseline			
				Summary		Individual		Summary		Individual	
	T	F	L	T	F	F	L	T	F	F	L
Proportion of Subjects with plasma HIV-1 RNA <50 c/mL at Week 24, 96 and 144 - Snapshot											
Week 24, 96 and 144 (ITT-E population)	Y						Y[1]				
Study Outcome [2] based on the Snapshot				Y[3]			Y				
By Visit	Y[4]				Y[5]						
Proportion of Subjects with plasma HIV-1 RNA <50 c/mL at Week 24, 48, 96 and 144 - Modified Snapshot											
Study Outcome [2] based on the Snapshot				Y[3]							
Proportion of Subjects with plasma HIV-1 RNA <200 c/mL at Week 24, 48, 96 and 144 - Snapshot											
Week 24, 48, 96 and 144 (ITT-E population)	Y						Y[1]				
Study Outcome [6] based on the Snapshot				Y[3]			Y				
By Visit	Y[4]				Y[7]						
Plasma HIV-1 RNA over time											
By Visit						Y[8]		Y[9]			
CD4+ Cell Counts and %											
By Visit						Y[8]	Y	Y	Y[10]		
CD8+ Cell Counts and %											
By Visit							Y	Y	Y		
CD4+/CD8+ Cell Count Ratio											
By Visit							Y	Y			
Confirmed Virologic Withdrawal (CVW)											
By Visit				Y							

Endpoints	Stats Analysis			Absolute				Change from Baseline			
				Summary		Individual		Summary		Individual	
	T	F	L	T	F	F	L	T	F	F	L
HIV-1 RNA distribution at time of suspected and confirmed Virologic withdrawal				Y							
HIV-1 RNA of subjects with at least one confirmed Virologic withdrawal visit							Y				
Post-baseline HIV-1 Disease Progression [11]											
HIV Conditions including Recurrences							Y				
HIV Conditions excluding Recurrences							Y				
HIV Disease Progressions							Y				

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. Listing of Quantitative and Qualitative Plasma HIV-1 RNA Data based on the snapshot algorithm.
2. Study outcomes (i.e. HIV-1 RNA >=50 c/mL, HIV-1 RNA <50 c/mL (response below 50 c/mL) or no virologic data at week x window) based on the snapshot algorithm.
3. Generated using the 'Intent-to-Treat Exposed'.
4. Including 95% confidence intervals.
5. Line plots, with 95% confidence intervals, for the proportion of subjects with HIV-1 RNA <50 c/mL at each visit.
6. Study outcomes (i.e. HIV-1 RNA >=200 c/mL, HIV-1 RNA <200 c/mL (response below 200 c/mL) or no virologic data at week x window) based on the snapshot algorithm.
7. Line plots, with 95% confidence intervals, for the proportion of subjects with HIV-1 RNA <200 c/mL at each visit.
8. Individual plasma HIV-1 RNA and CD4+ profiles for subjects with at least one CVW visit.
9. Descriptive summary of the log10 change from baseline HIV-1 RNA by visit presented.
10. Line plots, with 95% confidence intervals for Unadjusted Mean Change from Baseline in CD4+ Cell Count at each visit.
11. 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 1, 2 or 3 at enrolment to Death.

9.1.2. Planned Statistical Analyses

Secondary Efficacy Analyses
Endpoint(s)
• Proportion of participants with plasma HIV-1 RNA <200 and <50 c/mL at Week 24, Week 96 and Week 144.
Summary Measure
• Proportion of subjects within the ITT-E population with a plasma HIV-1 RNA <200 c/mL at visits will be presented, with focus on Week 24, Week 96 and Week 144 as a secondary endpoint of the study. • Proportion of subjects within the ITT-E population with a plasma HIV-1 RNA <50 c/mL at visits will be presented, with focus on Week 24, Week 96 and Week 144 as a secondary endpoint of the study.
Endpoint(s)
• Proportion of participants with plasma HIV-1 RNA <200 c/mL at Week 48.
Summary Measure
• The proportion of subjects within the ITT-E population with plasma HIV-1 RNA <200 c/mL at visits will be presented, with focus on Week 48 as a secondary endpoint of the study.
Endpoint(s)
• Change from baseline in CD4+ and CD8+ cell count and ratio at Week 24 and 48.
Summary Measure
• The absolute values of CD4+ and CD8+ cell count (cells/mm3) and the changes from baseline in CD4+ and CD8+ cell count (cells/mm3), with focus on Week 24 and Week 48. • Results will be presented for proportion of subjects with corresponding 95% CI (Mean ± 1.96 multiplied by the Standard Error of the Mean).

Supportive and Sensitivity Statistical Analyses
1. ITT-E Sens 1 population analysis: • To assess the impact after removal of participants with an absence of Week 48 data from one site in Kenya which was closed following sponsor investigation of significant quality issues. These results will be compared with the results from the ITT-E population. 2. ITT-E Sens 2 population analysis: • To assess the impact after removal of all participants from one site in Kenya which was closed following sponsor investigation of significant quality issues. These results will be compared with the results from the ITT-E population.

9.2. Safety Analyses

9.2.1. Overview of Planned Safety Analyses

The safety analyses will be based on the Safety population, unless otherwise specified. Post-Baseline Adverse Events will be tabulated by treatment group and time period (Up to Week 24, Up to Week 48, Up to Week 96, Up to Week 144 and Overall/All Available Data). Assessment windows per Appendix 14.3 will be used to determine inclusion in presentations with an Adverse Event (AE) included if the onset day is on or before the last day of the visit window of interest. Accordingly, AEs with onset days up to and including study day 210, 378, 714, and 1050 will be included in presentations of AEs up to Weeks 24, 48, 96, and 144, respectively. 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.

Table 5 provides an overview of the planned safety analyses, with further details of data displays being presented in Appendix 14.11: List of Data Displays.

Table 5 Overview of Planned Safety Analyses

Endpoint	Absolute				Change from Baseline		Max Post BL		
	Summary		Individual		Summary		Summary		
	T	F	F	L	T	F	T	F	L
Exposure									
Extent of Exposure	Y			Y[1]					
Adverse Events (AEs)									
All AEs by SOC and PT	Y			Y					
All AEs by SOC, PT and Maximum Toxicity [2]	Y								
Drug-Related AEs by SOC and PT	Y								
Drug-Related AEs by Maximum Toxicity [2]	Y								
AEs Experienced by >=2 Subjects by Frequency	Y								
Toxicity Grade 2-5 AEs by Frequency	Y								
Summary of Common (>=5%) Non-Serious AEs by SOC and PT (Number of Subjects and Occurrences)	Y								
Drug-Related Toxicity Grade 2-5 AEs by Frequency	Y								
Subject Numbers for Individual AEs				Y					
Relationship Between AE SOCs, PT and Verbatim Text				Y					

Endpoint	Absolute				Change from Baseline		Max Post BL		
	Summary		Individual		Summary		Summary		
	T	F	F	L	T	F	T	F	L
Cumulative AEs and Treatment-Related AEs	Y[3]								
Serious and Other Significant AEs									
SAEs by SOC and PT	Y								
Drug-Related SAEs by SOC	Y								
Serious Fatal and Non-Fatal Drug-Related AEs by Overall Frequency	Y			Y					
AEs Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	Y			Y					
Serious AEs by SOC and PT (Subjects & No. of Occurrences)	Y								
Reasons for Considering as a SAE				Y					
Possible Suicidality-Related Adverse Event (PSRAE)				Y[4]					
Impact of Covid-19 on Assessment of Safety Based on COVID-19 eCRF									
COVID-19 Assessments for Subjects with Suspected, Probable or Confirmed COVID-19 Case Diagnosis	Y								
COVID-19 Assessments and Symptom Assessments for Subjects with COVID-19 Adverse Events				Y					
Laboratory Values									
Clinical Chemistry	Y[3]			Y[5]	Y				
Fasting Lipids	Y[3]				Y				
Hematology	Y[3]			Y[5]	Y				
Urinalysis	Y[3]			Y[5]	Y				
Liver Chemistries								Y[6]	Y
Renal Chemistries			Y[7]						
Emergent Laboratory Toxicities[8]									
Clinical Chemistry							Y		
Hematology							Y		
Other									
ECG [9]				Y					
Vital Signs at Screening				Y[10]					
Hepatobiliary Abnormality criteria				Y					
Columbia suicidality	Y[11]			Y[12,13]					
Tanner Staging Score	Y			Y	Y				
Height, Weight and BMI Z-Scores[14]	Y			Y[10]	Y				
Subjects who became Pregnant				Y					
Patient Profiles				Y[15]					

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. Includes reason for any dose change/interruption.
2. For AEs reported more than once by a subject, the most severe intensity will be included.
3. Summary table displayed by visit.
4. Four PSRAE listings: Event and Description (Section 1-Section 2), Possible Cause (Section 3), Section 4 and Section 5-Section 8.
5. Listings for laboratory parameters with abnormalities of potential clinical concern, defined as any Grade 1-5 toxicity.
6. Scatter plot of baseline vs. maximum post-baseline for ALT. Scatter plot of maximum ALT vs. maximum Bilirubin.
7. Line Plot of Median (IQR) Serum Creatinine & eGFR Over Time.
8. Emergent Laboratory Toxicities.
9. Only collected at Screening or when a Cardiovascular event occurs.
10. Listing combines Vital Signs at Screening with Height, Weight and BMI (actual values only).
11. Includes: Summary of True Positive Suicidal Alerts Based on CSSRS by Visit, Summary of Subjects with C-SSRS Suicidal Ideation or Behavior at Baseline and Summary of Subjects with Post-Baseline C-SSRS Suicidal Ideation or Behavior.
12. Includes Baseline and lists all visits for a subject who reports any ideation or behaviour at any visit.
13. Separate outputs: Listing of False Positive Alerts with Corresponding Reasons and Listing of True Positives but not AEs with Corresponding Reasons.
14. Z-scores will not be included for the Week 48 analysis but will be considered for subsequent analysis timepoints.
15. Patient profiles for subjects with CVW. Patient profiles can also be provided for any other subjects, as necessary for medical review.

9.2.2. Planned Safety Statistical Analyses

Safety Statistical Analyses
Endpoint
• Incidence and severity of AEs and laboratory abnormalities through 144 weeks.
Summary Measure
• Proportion, number of events and severity of AEs and laboratory abnormalities based on the Safety Population up to Weeks 24, 48, 96 and 144.
Endpoint
• Proportion of participants who discontinue treatment due to AEs through 144 weeks.
Summary Measure
• The proportion of participants who discontinue treatment due to AEs based on the Safety Population up to Weeks 24, 48, 96 and 144.

Sensitivity Safety Statistical Analyses
1. Safety Sens 1 population: • To assess the impact after removal of participants with an absence of Week 48 data from one site in Kenya which was closed following sponsor investigation of significant quality issues. These results will be compared with the results from the Safety population. 2. Safety Sens 2 population: • To assess the impact after removal of all participants data from one site in Kenya which was closed following sponsor investigation of significant quality issues. These results will be compared with the results from the Safety population.

9.3. Viral Genotyping/Phenotyping

To assess the development of HIV-1 resistance in subjects who meet confirmed virologic withdrawal criteria, the incidence of treatment emergent genotypic and phenotypic resistance to DTG or 3TC in subjects meeting confirmed virologic withdrawal criteria will be listed using the ITT-E Population.

The virology analyses of genotype and phenotype data will be based on the CVW resistance population. Please see section 14.6.4 for details of the derivation of CVW.

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. Listings will present CVWs occurring at any point.

Table 6 provides an overview of the planned virology analyses, with full details of data displays being presented in Appendix 14.11: List of Data Displays.

Table 6 Overview of Planned Virology Analyses

Endpoint	Absolute			
	Summary		Individual	
	T	F	F	L
Summary of Subject Accountability				
Genotypes Available	Y			
Phenotypes Available	Y			
Genotypic resistance				
All Genotypic Data				Y
Genotypic results at Baseline and CVW [1]	Y [2]			Y [3]
Incidence of treatment-emergent genotype at time of CVW [1]	Y [2]			
Phenotypic resistance				
All Phenotypic Data				Y
Incidence of treatment-emergent phenotype at time of CVW [1]	Y [4]			Y
Replication capacity				Y
Fold Change at Baseline and CVW	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 suspected visit date, and only tested once a subject confirms virological failure at a subsequent visit.
2. Separate outputs for INI and NRTI/NNRTI/PI mutations.
3. All and Treatment Emergent.
4. Separate outputs by phenotypic cut-off and by number of drugs to which subjects are resistant.

10. EXPLORATORY ANALYSIS

As an exploratory and supportive analysis, a retrospective Bayesian Dynamic Borrowing analysis will be performed for the primary efficacy endpoint which will make use of available adult information from two previous studies to inform the paediatric data being collected in this study. Details of the planned analysis will be documented separately.

11. PHARMACOKINETIC ANALYSES

11.1. Overview of Planned Pharmacokinetic Analyses

All PK concentration listing displays will be based on the Intensive and Sparse + Trough Pharmacokinetic populations. Concentrations of DTG and 3TC in plasma will be listed and summarized according to GSK standards, where applicable (Refer to Appendix 5: Data Display Standards & Handling Conventions

(Section 14.5.2 Reporting Standards for Pharmacokinetic)).

DTG and 3TC concentration listings for the intensive PK population will be sorted by subject and time relative to dose, noting the study visit; summaries will be presented by time relative to dose.

DTG and 3TC concentration listings for the sparse + trough PK population will be sorted by subject, study visit and time (or sampling window) relative to dose; summaries will be presented by study visit and sampling window for Weeks 4, 12, and 24 (sparse PK) and for Weeks 8, 16, 36 and 48 (trough PK). For the intensive population, PK samples with protocol deviations for DTG and 3TC can be included for the purpose of summary statistics if

- Samples collected 1 hour prior to dose for pre-dose sample
- Samples collected within ±15 min of the 0.5, 1, 1.5, 2 H time points
- Samples collected within ± 30 min of the 3h, 4h, 6h time points
- Samples collected within ± 1h for the 10h time point
- Samples collected within ± 2h for the 24 h time point.

Outside these allowed windows, concentration results will be flagged and NOT included in the calculations for the summaries.

Results based on samples collected from a participant with emesis within 4 hours of the dose will be flagged in the PK concentration and PK parameter listings and excluded from table summaries and mean and median figures.

Table 7 Overview of Planned Pharmacokinetic Analyses

End Point	Untransformed							Log-Transformed			
	Stats Analysis			Summary		Individual		Summary		Individual	
	T	F	L	T	F	F	L	T	F	F	L
Intensive PK Concentrations											

End Point	Untransformed							Log-Transformed			
	Stats Analysis			Summary		Individual		Summary		Individual	
	T	F	L	T	F	F	L	T	F	F	L
Plasma 3TC Concentrations				Y	Y [2]	Y [1]	Y		Y [2]	Y [1]	
Plasma DTG Concentrations				Y	Y [2]	Y [1]	Y		Y [2]	Y [1]	
Sparse + Trough PK Concentrations											
Plasma 3TC Concentrations by Visit and sampling window				Y		Y	Y		Y		
Plasma DTG Concentrations by Visit and sampling window				Y		Y	Y		Y		
Intensive PK Parameters											
Plasma 3TC Parameters				Y			Y	Y			
Plasma DTG Parameters				Y			Y	Y			

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 Linear and Semi-Log plots will be created.
2 Mean plots on linear and semi-log scale will be generated.

11.2. Drug Concentration Measurements

Refer to Appendix 5: Data Display Standards & Handling Conventions

(Reporting Process & Standards).

11.3. Pharmacokinetic Parameters

- Refer to Appendix 5: Data Display Standards & Handling Conventions
- (Reporting Process & Standards).
- For participants in the Intensive Pharmacokinetic population, the PK parameters will be calculated by standard non-compartmental analysis according to current working practices and using Phoenix WinNonlin® (WNL) 8.0 or higher (Pharsight

Corporation, a Certara Company, Princeton, NJ), and/or SAS® Version 9.3 or higher. Graphics will be prepared using the same version of SAS®.

- All calculations of non-compartmental parameters will be based on actual sampling times.

From the plasma concentration-time data, the following pharmacokinetics parameters of DTG and 3TC at steady state will be determined as data permit:

Parameter	Parameter Description
$AUC_{(0-\tau)}$	Area under the concentration-time curve over the dosing interval (ng·h/mL), calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
C_{max}	Maximum observed concentration in plasma (ng/mL), determined directly from the concentration-time data.
t_{max}	Time to reach C_{max} (h), determined directly from the concentration-time data.
C_0	Observed pre-dose concentration
C_{24}	Concentration in the plasma at 24 hours after dosing (ng/mL), obtained from the observed concentration versus time data.
$t_{½}$	Apparent terminal half-life (h) will be calculated as: $t_{½} = \ln 2 / \lambda_z$
λ_z	Apparent terminal rate constant (1/h), determined by linear regression of the terminal points of the log-linear concentration-time curve. Visual assessment will be used to identify the terminal linear phase of the concentration-time profile. A minimum of 3 data points will be used for determination.

NOTES:

- Additional parameters may be included as required.
- If less than three time points are available (post C_{max}), then λ_z and $t_{1/2}$ will not be calculated or reported.

12. POPULATION PHARMACOKINETIC (POPPK) ANALYSES

Population PK analyses are not applicable to analyses post Week 48.

If data permits, the sparse and trough sample concentrations of 3TC and DTG collected at Weeks 4, 8, 12, 24, 36 and 48 will be pooled with the intensive PK concentrations and potentially data from other studies to perform integrated PK analyses for DTG and 3TC. The primary goal of this analysis is to characterize the population pharmacokinetics of 3TC and DTG administered as a dual regimen maintenance treatment for HIV in participants who are virologically suppressed. The influence of subject demographics, baseline characteristics, including disease activity, and co-medication on the pharmacokinetics of 3TC and DTG in this population will be investigated. The individual subject PK parameters will be estimated, and the corresponding exposure metrics will be compared with that of adults. The PopPK analyses for DTG and 3TC will be performed under a separate RAP and will be reported separately.

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14. APPENDICES

Section	Appendix
RAP Section 6 : General Considerations for Data Analyses & Data Handling Conventions	
Section 14.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population • Exclusions from Per Protocol Population
Section 14.2	Appendix 2: Time & Events • Protocol Defined Time & Events
Section 14.3	Appendix 3: Assessment Windows • Definitions of Assessment Windows for Analyses • Definitions of Assessment Windows for Inclusion in the PK Analysis • Multiple Assessments • Invalid Laboratory Assessments • Abnormalities of Potential Clinical Concern • Classification of Prior, Concomitant, and Post-Therapy Medications
Section 14.4	Appendix 4: Treatment States and Phases • Treatment Phases and States • Treatment States for AE Data
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Section	Appendix
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14.1. Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population

14.1.1. Exclusions from Per Protocol Population

A subject meeting any of the Significant Protocol Deviations detailed in the Protocol Deviation Rule Document will be excluded from the Per Protocol population.

14.2. Appendix 2: Time & Events

14.2.1. Protocol Defined Time & Events

Procedure	Screening[a]	Treatment Phase (Week)									Extension Phase[b]	Continuation Phase[c]	End Continuation Phase Visit	Withdrawal[d]	Follow Up[e]	Notes
		Baseline/ Day 1	1	4	8	12	16	24	36	48	Every 12 weeks after Week 48 through Week 144	Every 12 weeks after Week 144				
[a] **Screening**: Enrolment may occur as soon as all Screening results are available. [b] **Extension Phase**: All participants who successfully complete treatment through Week 48 will have the opportunity to enter the Extension Phase. [c] **Continuation Phase**: If required by local regulations, study participants who have successfully completed the study through Week 144 may enter the Continuation Phase, regardless of age, and will continue to receive DTG/3TC until it is available locally (See Protocol Section 7.10, Treatment after the End of the Study). Prior to transitioning to locally approved and available supply, the participant will return to complete a final End of Continuation Phase visit. [d] **Withdrawal**: Participants will complete a Withdrawal visit at the time they withdraw from the study and will return for a follow-up visit 4 weeks after the last dose of study medication. [e] **Follow-up:** An in-clinic Follow-Up visit will be conducted 4 weeks after the last dose of study medication upon withdrawal from study. A follow-up visit will not be applied for participants completing the End of Continuation Phase Visit, (as they will continue to receive DTG plus 3TC) or for participants who withdraw consent for further participation at the time of early withdrawal from the study.															
Clinical and Other Assessments																

Procedure	Screening[a]	Treatment Phase (Week)									Extension Phase[b]	Continuation Phase[c]	End Continuation Phase Visit	Withdrawal[d]	Follow Up[e]	Notes
		Baseline/ Day 1	1	4	8	12	16	24	36	48	Every 12 weeks after Week 48 through Week 144	Every 12 weeks after Week 144				
Written informed consent and assent[e]	SC	.	.	.	.	.	.	.	.	.	.	.	.	.	.	Assent will be obtained as appropriate according to local guidelines. Written informed consent must be obtained from the participant if he/she reaches the age of majority while on study.
Inclusion and exclusion criteria	SC	B	.	.	.	.	.	.	.	.	.	.	.	.	.	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.
Demography	SC	.	.	.	.	.	.	.	.	.	.	.	.	.	.	Including year of birth, sex, race, ethnicity.

Procedure	Screening[a]	Treatment Phase (Week)									Extension Phase[b]	Continuation Phase[c]	End Continuation Phase Visit	Withdrawal[d]	Follow Up[e]	Notes
		Baseline/ Day 1	1	4	8	12	16	24	36	48	Every 12 weeks after Week 48 through Week 144	Every 12 weeks after Week 144				
Medical history (includes substance abuse)	SC	.	.	.	.	.	.	.	.	.	.	.	.	.	.	Full medical history will be conducted prior to enrollment 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.
Prior ART/PMTCT history, as applicable	SC	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
Tanner staging score	.	B	.	.	.	.	.	.	.	48	E (Every 48 Weeks)	.	.	.	.	Tanner scoring will be collected until the end of adolescence. During the Extension Phase, assess Tanner Score only every 48 weeks.
Concurrent medical conditions	SC	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
Vital signs	SC	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
HIV risk factors and mode of transmission	.	B	.	.	.	.	.	.	.	.	.	.	.	.	.	

Procedure	Screening[a]	Treatment Phase (Week)									Extension Phase[b]	Continuation Phase[c]	End Continuation Phase Visit	Withdrawal[d]	Follow Up[e]	Notes
		Baseline/ Day 1	1	4	8	12	16	24	36	48	Every 12 weeks after Week 48 through Week 144	Every 12 weeks after Week 144				
CDC or WHO HIV-1 classification	SC	B	.	.	.	.	.	.	.	.	.	.	.	.	.	See Protocol Section 12.6, Appendix 6: CDC Classification and WHO Staging for HIV-1 Infection
HIV associated conditions	.	.	.	4	8	12	16	24	36	48	E	C	EC	W	.	
Columbia Suicidality Rating Scale	.	B	.	4	8	12	16	24	36	48	E	C	EC	W	.	On Day 1, the electronic Columbia Suicidality Severity Rating Scale eCSSRS, (patient completed questionnaire) is to be administered prior to enrolment. CSSRS participant level reports should reviewed, signed by Investigator or Sub-Investigator and filed in site source. Actions taken for positive findings should be clearly documented.
Concomitant medication	SC	B	.	4	8	12	16	24	36	48	E	C	EC	W	F	

Procedure	Screening[a]	Treatment Phase (Week)									Extension Phase[b]	Continuation Phase[c]	End Continuation Phase Visit	Withdrawal[d]	Follow Up[e]	Notes
		Baseline/ Day 1	1	4	8	12	16	24	36	48	Every 12 weeks after Week 48 through Week 144	Every 12 weeks after Week 144				
Symptom directed physical examination/Medical decision making including height and weight	SC	B	.	4	8	12	16	24	36	48	E	.	.	W	F	
12-lead ECG	SC	.	.	.	.	.	.	.	.	.	.	.	.	.	.	Perform 12-lead ECG after resting in a semi-supine position for at least 5 minutes.
Adverse events	SC	B	.	4	8	12	16	24	36	48	E	C	EC	W	F	Only SAEs related to study participation or to a concomitantly administered ViiV Healthcare/GlaxoSmithKline (GSK) product will be collected between obtaining informed consent and administration of study drug at Day 1.
Serious adverse events	SC	B	.	4	8	12	16	24	36	48	E	C	EC	W	F	
Laboratory Assessments																
Plasma for HIV genotyping	SC	.	.	.	.	.	.	.	.	.	.	.	.	.	.	

Procedure	Screening[a]	Treatment Phase (Week)									Extension Phase[b]	Continuation Phase[c]	End Continuation Phase Visit	Withdrawal[d]	Follow Up[e]	Notes
		Baseline/ Day 1	1	4	8	12	16	24	36	48	Every 12 weeks after Week 48 through Week 144	Every 12 weeks after Week 144				
Quantitative plasma HIV-1 RNA	SC	B	.	4	8	12	16	24	36	48	E	C	EC	W	.	
Lymphocyte subsets	SC	B	.	4	8	12	16	24	36	48	E	.	.	W	.	
Plasma for storage	SC	B	.	4	8	12	16	24	36	48	E	C	EC	W	.	Plasma samples for storage will be collected at each visit starting at Screening, including any unscheduled visits. These samples will be used when needed such as when samples are lost, arrive at the laboratory unevaluable, or for PK or genotypic and/or phenotypic analyses when participants meet Suspected and Confirmed Virologic Withdrawal criteria.
Clinical chemistry	SC	B	.	4	8	12	16	24	36	48	E	.	.	W	F	
Hematology	SC	B	.	4	8	12	16	24	36	48	E	.	.	W	F	
PT/INR	SC	.	.	.	.	.	.	.	.	.	.	.	.	.	.	

Procedure	Screening[a]	Treatment Phase (Week)									Extension Phase[b]	Continuation Phase[c]	End Continuation Phase Visit	Withdrawal[d]	Follow Up[e]	Notes
		Baseline/ Day 1	1	4	8	12	16	24	36	48	Every 12 weeks after Week 48 through Week 144	Every 12 weeks after Week 144				
Fasting lipids, glucose, HbA1c	.	B	.	.	.	.	.	24	.	48	E	.	.	W	.	An overnight fast is preferred; however, a minimum of a 6-hour fast is acceptable. During Extension Phase, collect fasting lipids, glucose, and glycated haemoglobin (Hb1Ac) only every 24 weeks. Collect at Withdrawal only if withdrawal visit occurs at Weeks 48,96 or 144
Urinalysis and spot urine for protein analysis	.	B	.	.	.	12	.	24	.	48	E	.	.	W	F	A morning specimen is preferred

Procedure	Screening[a]	Treatment Phase (Week)									Extension Phase[b]	Continuation Phase[c]	End Continuation Phase Visit	Withdrawal[d]	Follow Up[e]	Notes
		Baseline/ Day 1	1	4	8	12	16	24	36	48	Every 12 weeks after Week 48 through Week 144	Every 12 weeks after Week 144				
Pregnancy test	SC (S)	B (U)	.	4 (S)	8 (S)	12 (S)	16 (S)	24 (S)	36 (S)	48 (S)	E (S)	C (S)	EC (S)	W (S)	.	Pregnancy testing will be conducted (females of reproductive potential only) on serum (S) samples with the exception of Day 1, which must be a urine (U) test to confirm status prior to administration of study treatment. Remind females of reproductive potential of the need to avoid pregnancy while in study and adherence to the study's contraception requirements.
HBsAg, anti-HBc, anti-HBs, and HBV DNA	SC	.	.	.	.	.	.	.	.	.	.	.	.	.	.	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 will have to return to the clinic to provide a sample for HBV DNA testing prior to enrollment.
HCV antibody	SC	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
RPR	SC	.	.	.	.	.	.	.	.	.	.	.	.	.	.	

Procedure	Screening[a]	Treatment Phase (Week)									Extension Phase[b]	Continuation Phase[c]	End Continuation Phase Visit	Withdrawal[d]	Follow Up[e]	Notes
		Baseline/ Day 1	1	4	8	12	16	24	36	48	Every 12 weeks after Week 48 through Week 144	Every 12 weeks after Week 144				
Sample for Ctrough measurement	.	.	.	.	8	.	16	.	36	48	.	.	.	.	.	
Sample for pharmacokinetic analysis (sparse collection – all participants)	.	.	.	4	.	12	.	24	.	.	.	.	.	.	.	At each scheduled visit, collect a predose sample and a post dose sample as described in Protocol Section 9.6.1
Dispense PK Diary Card	.	B	.	4	8	12	16	24	36	48	.	.	.	.	.	Participant to complete dosing diary for 3 days prior to PK and Ctrough sampling visits. The PK visit should be re-scheduled if the participant took their morning dose prior to coming into the clinic on the sparse or intensive PK sampling day.
Sample for pharmacokinetic analysis (intensive serial collection – subset of participants)	.	.	1	.	.	.	.	.	.	.	.	.	.	.	.	To be collected in a subset of participants between Days 5 and 10. Samples will be drawn between days 5 and 10 at the following timepoints: predose, 0.5, 1, 1.5, 2, 3, 4, 6,10, and 24 hours post dose. See Protocol Section 9.6.2.3.

Procedure	Screening[a]	Treatment Phase (Week)									Extension Phase[b]	Continuation Phase[c]	End Continuation Phase Visit	Withdrawal[d]	Follow Up[e]	Notes
		Baseline/ Day 1	1	4	8	12	16	24	36	48	Every 12 weeks after Week 48 through Week 144	Every 12 weeks after Week 144				
Dispense Intensive PK Diary Card to Intensive PK sub-set	.	B	.	.	.	.	.	.	.	.	.	.	.	.	.	Participant to complete dosing diary for 3 days prior to PK sampling visit. The PK visit should be re-scheduled if the participant took their morning dose prior to coming into the clinic on the intensive PK sampling day.
Whole blood sample (virology)	.	B	.	.	.	.	.	.	.	48	E (at Week 144)	.	.	W	F	Whole blood (Virology) may be used for virologic analyses as described in the protocol. In the Extension Phase, collect only at Week 144.
Study Treatment																
IVRS/IWRS	SC	B	1	4	8	12	16	24	36	48	E	C	EC	W	F	
Dispense study medication	.	B	.	4	8	12	16	24	36	48	E	C	.	.	.	Medication may be dispensed until the participant's last on study visit.
Study medication accountability	.	.	.	.	8	12	16	24	36	48	E	C	EC	W	.	

anti-HBc = antibody to hepatitis B core antigen, anti-HBs = hepatitis B surface antibody, ART = antiretroviral therapy, B= Baseline, C= Continuation Phase, CDC = Centers for Disease Control and Prevention, DNA = deoxyribonucleic acid, E = Extension Phase Visit, EC= End of Continuation Phase Visit, ECG = electrocardiograph, F= Follow-up Visit, HBsAg = hepatitis B surface antigen, HCV = hepatitis C virus, HIV-1 = human immunodeficiency virus type 1, INR = international normalized ratio, IVRS = interactive voice recognition system, IWRS = interactive web recognition system, PMTCT = prevention of mother to child transmission, RNA = ribonucleic acid, RPR = rapid plasma reagin, SC= Screening, W= Withdrawal Visit

14.3. Appendix 3: Assessment Windows

14.3.1. Definitions of Assessment Windows for Analyses

Withdrawal date from IP/investigational product, laboratory data, vital signs, 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.

Based on the Study Day (see Section 14.6), assessments are assigned as shown in Table 8.

Table 8 Assessment Windows

Analysis Set / Domain	Parameter (if applicable)	Target	Analysis Window		Analysis Timepoint
			Beginning Timepoint	Ending Timepoint	
All	All	-35	≤-4	≤-4	Screening
		1	-3	1	Day 1
		29	2	42	Week 4
		57	43	70	Week 8
		85	71	98	Week 12
		113	99	140	Week 16
		169	141	210	Week 24
		253	211	294	Week 36
		337	295	378	Week 48
		421	379	462	Week 60
		7*w+1	7*w-41	7*w+42	Week w, w=72, 84, 96, ...
		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).

14.3.2. Definitions of Assessment Windows for Inclusion in the PK Analysis

The windows for inclusion of PK samples in summary statistics will be as follows:

- For intensive PK population (Week 1 only):
    - Samples collected 1 hour prior to dose for pre-dose sample
    - Samples collected within ±15 min of the 0.5, 1, 1.5, 2 H time points
    - Samples collected within ± 30 min of the 3h, 4h, 6h time points
    - Samples collected within ± 1h for the 10h time point
    - Samples collected within ± 2h for the 24 h time point
- For sparse + trough PK population (Weeks, 4, 8, 12, 16, 24, 36 and 48):
    - Samples collected within 1 hour prior to dose for pre-dose sample, within ±30 min window for 2-4hr post dose sample (i.e. between 1.5-4.5hr), within ±60 min window for 4-12hr post dose sample (i.e. between 3-13hr) and within ±120 min window for 12-24hr post dose sample (i.e. between 10-26hr).

Outside these allowed windows, concentration results will be flagged and NOT included in the calculations for the summaries, but will be used in listings.

Given steady state will be reached by Day 5, sparse PK analyses will use nominal visit windows for all sparse PK analyses.

14.3.3. Multiple Assessments

If after window assignment there are multiple valid (see Section 14.3) assessments of a parameter within the same window and associated with the scheduled Study Phase, then the following hierarchy will be used to determine the value to be used for summary statistics of observed values for those which did not occur at Screening or Day 1:

- The assessment closest to the window target Study Day.
- If there are central and local lab parameter results with the same sample collection date, select the central lab value.
- 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 worst value. For HIV-1 RNA, the geometric mean of the number of copies will be used as opposed to the arithmetic mean.

For multiple valid assessments of a parameter occurring at Screening or Day 1:

- If there are central and local lab results for the same parameters with the same sample collection date, select the central lab value.
- If there are multiple assessments within the Screening window, select the last assessment before Day 1.
- If there are multiple assessments within the Day 1 window, select the latest pre-dose assessment.

Assessments not chosen for use in summary statistics by these algorithms will still appear in the associated listings. Also, such valid assessments will be used when determining abnormalities 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).

14.3.4. Invalid Laboratory Assessments

Certain laboratory endpoints are required to be collected in a fasting state, i.e., glucose and lipids (triglycerides, total cholesterol, HDL, LDL). If these endpoints are collected in a non-fasting state, then the results will be excluded from summaries; such results will be included in data listings with the fasting status noted.

14.3.5. Abnormalities of Potential Clinical Concern

The DAIDS grading for severity of laboratory toxicities and clinical adverse events is included in the protocol (Appendix 7, Section 12.7). The central laboratory will flag lab parameter toxicities directly in the provided datasets.

14.3.6. Classification of Prior, Concomitant, and Post-Therapy Medications

Prior medications are those taken (i.e., started) before the start date of Investigational product. Concomitant medications are those taken (i.e., started or continued) at any time between the start date and stop date of IP, inclusive. Prior medications that were continued during this period are also considered as concomitant medications. Post-treatment medications are those started after the stop date of IP. 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. Also, for any medication starting on the same date as IP, it will be assumed that the medication was taken after the subject started taking IP.

Table 9 illustrates how a medication is classified as prior, concomitant, or post-treatment.

Table 9 Prior, Concomitant, and Post-treatment Classification of Medications

	Pre-treatment	On-treatment			Post-treatment		Prior	Conco-mitant	Post
		IP Start Date		IP Stop Date	IP Stop Date+1				
(a)	x————						Y	N	N
(b)	x————.		————x				Y	Y	N
(c)	x————.		————			————x	Y	Y	Y
(d)			x————x				N	Y	N
(e)			x————			————x	N	Y	Y
(f)						x————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.

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

- if the partial date is a start date, a '01' will be used for missing days and 'Jan' will be used for missing months;
- if the partial date is a stop date, a '28/29/30/31' will be used for the missing day (dependent on the month and year) and 'Dec' will be used for missing months; for medications recorded in the eCRF as prior antiretroviral therapy (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.

Study Population Analyses
Concomitant Medications
• For reporting purposes, medications will be classified as prior, concomitant, and/or post-treatment using the associated start and stop dates recorded in the eCRF and relative to the first and last dose dates of investigational product (see Section 14.3.6). Medications will be coded using the GSK Drug coding dictionary. • This display will also include single-ingredient medications. Multi-ingredient medications will be labelled according to the sum of their ingredients, e.g., "TYLENOL Cold and Flu" would appear as "CHLORPHENAMINE MALEATE + DEXTROMETHORPHAN HYDROBROMIDE + PARACETAMOL + PSEUDOEPHEDRINE HYDROCHLORIDE" under the ATC headings for "Nervous System" and "Respiratory System" (the combination's ATC classifications).
Prior and Concomitant Antiretroviral Therapy (ART)
• ART medications will be classified as prior, concomitant, and/or post-treatment according to Section 14.3.6, with the following modifications: o ART starting on IP stop date will be considered as only post-treatment and not concomitant. It is expected that after discontinuation of IP, a subject may immediately begin taking another ART. o ART stopping on IP start date will only be considered as prior and not concomitant. o Any ART entered on the Prior ART eCRF with missing or partial end date will be assumed to have finished before Screening. • Summaries of ART will be grouped by GSK Drug ATC classification level 4 (which will provide ART class). Classes are Integrase (inhibitor) (INI), NRTI, Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI), Protease inhibitor (PI) and Other. LAMIVUDINE should be grouped into NRTI.

14.4. Appendix 4: Treatment States and Phases

14.4.1. Treatment Phases and States

Assessments and events will be classified according to time of occurrence relative to the start and/or stop date of IP as either Pre-treatment, On-treatment or Post-treatment.

For laboratory data, HIV, vital signs, and genotypic and phenotypic data, treatment state will be defined as in Table 10.

Table 10 Treatment State for Laboratory Data, HIV Associated Conditions, Vital Signs, and Genotypic and Phenotypic Data

Treatment Phase	Treatment State	Definition
Treatment Phase	Pre-Treatment	date ≤ IP Start Date
	On-Treatment	IP Start Date < date ≤ Week 48 Date of Visit (DOV) or if withdrawn prior to or at Week 48: IP Start Date < date ≤ IP Stop Date + 1
	Post-Treatment (withdrawn prior to Week 48 or not enter the Extension)	date > IP Stop Date + 1
Extension Phase	On-Treatment	Week 48 DOV < date ≤ Week 144 DOV or if withdrawn prior to Week 144: IP Start Date ≤ date ≤ IP Stop Date + 1
	Post-Treatment (withdrawn prior to Week 144 or not enter the Continuation)	date > IP Stop Date + 1
Continuation Phase	On-Treatment	Week 144 DOV < date ≤ IP Stop Date +1
	Post-Treatment	date > IP Stop Date + 1> Week 144 DOV

If the IP Stop Date for any study phase is completely missing, then any assessment after that IP Start Date will be considered to be On-treatment for that study phase.

14.4.1.1. Treatment States for AE Data

For adverse events, treatment state will be defined as in Table 11, where a partial AE start date uses imputation as described in Section 14.7.2.1. 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.

Table 11 Treatment State for Adverse Events

Study Phase	Treatment State	Assessment/Start Date vs. IP Start/Stop Date
Treatment Phase	Pre-Treatment	date < IP Start Date
	On-Treatment	IP Start Date ≤ date ≤ Week 48 DOV or if withdrawn prior to Week 48: IP Start Date ≤ date ≤ IP Stop Date
	Post-Treatment (withdrawn prior to Week 48 or not enter the Extension Phase)	date > IP Stop Date
Extension Phase	On-treatment	Week 48 DOV < date ≤ Week 144 DOV or if withdrawn prior to Week 144: IP Start Date ≤ date ≤ IP Stop Date
	Post-Treatment (withdrawn prior to Week 144 or not enter the Continuation)	date > IP Stop Date
Continuation Phase	On-Treatment	Week 144 DOV < date ≤ IP Stop Date
	Post-Treatment	date > IP Stop Date > Week 144 DOV

If the IP Stop Date for any study phase is completely missing, then any event with a start date on or after IP Start Date will be considered to be On-treatment for that study phase. If the start date of the AE for any study phase is after IP Stop Date for that study phase but has been recorded as potentially related to IP, then it will be classified as On-treatment for that study phase.

For reporting purposes, prior, concomitant, and follow-up medications will be classified according to treatment states defined in Section 14.3.6.

14.5. Appendix 5: Data Display Standards & Handling Conventions

14.5.1. Baseline Definition & Derivations

Unless stated otherwise, the baseline value for a parameter (including labs, vital signs, virology assessments, etc.) is defined as the last Pre-treatment value observed. This is generally expected to be from the Day 1 visit, although such values may be missing or unscheduled assessments may be performed before treatment start. If there are multiple assessments collected on the same scheduled time, the average of these assessments will be used. However, if for a lab parameter there are both central and local lab values with the same sample collection date, the central lab value will be used.

Change from baseline for a parameter is calculated as (observed value - baseline value).

The percentage change from baseline for a parameter is calculated as

$$\%\,\text{change from baseline} = \frac{\text{observed value} - \text{baseline value}}{\text{baseline value}} \times 100$$

14.5.2. Reporting Process & Standards

Reporting Process
Software
• The currently supported versions of SAS software 9.3 will be used.
Analysis Datasets
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 or higher & ADaM IG Version 1.1 or higher).   • 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 analyses.

Reporting Standards
General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated:
  o 4.03 to 4.23: General Principles.
  o 5.01 to 5.08: Principles Related to Data Listings.
  o 6.01 to 6.11: Principles Related to Summary Tables.
  o 7.01 to 7.13: Principles Related to Graphics.

Formats

Reporting Standards	
• GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DPs) will be adopted for reporting of data based on the raw data collected. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DPs.	
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 IDSL Statistical Principle 5.05.1).	

Unscheduled Visits	
• Unscheduled visits will be assigned to a study visit using the all-inclusive windows defined in Section 14.3. • 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 IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Reporting of Pharmacokinetic Parameters	
Descriptive Summary Statistics (Log Transformed)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of log-transformed data and between geometric coefficient of variation (CVb/w (%)) will be reported. [1] CV_b (%) = $\sqrt{}$ (exp(SD^2) – 1) * 100 (SD = SD of log transformed data)
Parameters Not Being Log Transformed	t_{max}, λ_z, λ_z lower, λ_z upper, λ_z and no. of points
Listings	Interval, number of observations included in calculation of λ_z, regression coefficient
Graphical Displays	
• Refer to IDSL Statistical Principles 7.01 to 7.13.	

14.5.3. Study Treatment Display Descriptors

Data Displays for Reporting Treatment Group Descriptions
Description
DTG / 3TC

14.6. Appendix 6: Derived and Transformed Data

14.6.1. General

Study Day
• The Study Day of an event (e.g., lab assessment, vital sign, and start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the initial start date of IP as follows: • Date of Event = Missing → Study Day = Missing • Date of Event < Start Date of IP → Study Day = Date of Event – Start Date of IP • Date of Event ≥ Start Date of IP → Study Day = Date of Event – (Start Date of IP) + 1
Post-baseline
• Post-baseline refers to the combined time periods of On-treatment and Post-treatment. (Appendix 4: Treatment States and Phases).
Emergent
• Emergent refers to AE Severity/ Lab toxicity that develops or increases in intensity after baseline.
Study Drug
• Study Drug refers to Investigation Product DTG/3TC.

14.6.2. 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 standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows: o Any subject with a missing date and month will have this imputed as '30th June'. o For analysis purposes, if a subject did not fail to meet inclusion criteria (aged between 12 and less than 18 years), then set any age imputed as 11 by the GSK Statistical Display Standard algorithm to 12 and any age imputed as 18 to 17. If the subject failed to meet inclusion criteria 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.
• Body Mass Index (BMI) will be calculated as weight (kg) at baseline / [height (m) at baseline]^2.

14.6.3. Safety

Extent of Exposure
• Number of days of exposure to study drug will be calculated based on the formula: Duration of Exposure in Days = IP Stop Date – (IP Start Date) + 1. where IP Stop Date is the date of final dose of IP received and IP Start Date is the date of initial dose of IP in the study. • The first and last doses and any changes/interruptions in dosing of investigator product will be listed for all subjects, together with details of the reason for any dose change/interruption. • 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. • Distribution and summary statistics for the duration of exposure to IP will be presented.
Adverse Events
Adverse Events
• 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 14.11: List of Data Displays. • Post-Baseline AEs will be tabulated. For Post-Baseline AEs captured more than once, the most severe intensity will be included in summaries, and all events will be included in listings. • Safety data presented through the timepoint of interest (i.e. up to Weeks 24, 48, 96 and 144), will comprise all available safety data collected up to the timepoint of the data cut for analysis. The cut-off date of each timepoint analysis will be defined as the ending timepoint of Analysis Window of the visit of the period to analyse (see Section 14.3.1). • Adverse events (AEs) will be coded using the most recent MedDRA coding dictionary to give a preferred term and a system organ class. These preferred terms and system organ classes will be used when summarising the data. The verbatim text will be used in listings together with the preferred term. A listing of the relationship of preferred term to verbatim text will be presented ordered by system organ class.
AE Severity – DAIDS Grading
• Toxicity grades will be based on the Division of Acquired Immunodeficiency Syndrome (DAIDS) grading system. The DAIDS grading (VERSION 2.1, March 2017) for severity of clinical adverse events will be performed. • See protocol for DAIDS grading criteria.
Adverse Events of Special Interest (AESI)
The discussion of any AESIs will be determined/discussed via the AE listings (no plan for either AESI summaries or AESI listings).
Suicidality Events
The number and percentage of subjects with a positive suicidal indication alert result by visit will be summarized, excluding any false positive results. A positive suicidal indication alert is where there is a 'Yes' result for a level, [redacted] or [redacted] ideation, or any suicidal behaviour. Ideation levels [redacted] and [redacted] are where there is ideation but importantly there is intent to act on it. An alert is then sent to the investigator which leads to follow-up with the participant to determine if the positive alert is 'true' or 'false' (essentially, does it truly indicate suicidality) and from that, if this should be recorded as an AE/SAE/PSRAE. A false positive alert is one where the site determines the subject does not have suicidal risk, and/or there was an error recorded onsite. A listing of subjects who experience possible depression and/or suicidality-related adverse events along with the data from the Columbia-Suicide Severity Rating Scale (C-SSRS) will be listed. The C-SSRS suicidal ideation and

behaviour data will also be listed, and a listing of false positive alerts with the investigator adjudication will also be provided.

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 CRF 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.
        - The exception to this is where an investigator's assessment of true positive alert (recorded in the eCRF) relates only to an earlier duplicate call. In such situations the earlier 'positive' alert will be selected over the later 'negative' assessment thus ensuring both the positive alert and the resulting true positive assessment by the investigator are selected for summary.
    - For summary tables at baseline, unscheduled repeat visits will not be summarised.
    - Relevant CRF pages will be completed based on the latest entry (if it was a positive alert).
- Baseline Selection:
    - Late DAY 1 assessments occurring by study day 14 will be considered for potential representation of baseline status. Of eligible DAY 1 assessments, a single DAY 1 assessment / questionnaire will be selected to represent baseline status. After application of rules relating to incomplete and duplicate records (see above), where multiple eligible DAY 1 assessments exist, selection will be based on the assessment satisfying the first of the following: (1) an assessment on study day 1, (2) the last assessment pre-study day 1, (3) the earliest assessment post-study day 1.
- Use of later DAY 1 assessment data:
    - 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 (i.e., these assessments will be considered to represent post-baseline findings and included in summaries accordingly).
- Post-Baseline selection:
    - Assessments using the 'Since last assessment' questionnaire will be considered to represent post-baseline assessments other than unscheduled assessments performed on study day 1 (i.e., those with a visit label of 'UNSCHEDULED - 20.01'). Although an unscheduled

assessment on study day 1 may be intended to represent baseline, the more complete DAY 1 assessment is selected for this purpose. As a result, such assessments will be listed but not summarised.

Clinical Laboratory Evaluations

Hematology

- platelet count, red blood cell (RBC) count, white blood cell (WBC) count, hemoglobin, hematocrit, mean corpuscle volume (MCV), mean cell hemoglobin (MCH) ;
- WBC differential (count and %): neutrophils, lymphocytes, monocytes, eosinophils, basophils.

Clinical chemistry

- liver chemistries: alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, alkaline phosphatase (ALP);
- electrolytes: sodium, phosphate, chloride, potassium, calcium;
- renal chemistries: blood urea nitrogen (BUN), creatinine, and GFR - estimated by the central laboratory using the Bedside Schwartz equation [Schwartz, 2009]. In addition, GFR will be estimated by the central laboratory using Creatinine-Cystatin C-Based CKiD Equation [Schwartz, 2012] at day 1 and when indicated by renal toxicity criteria.
- other: protein, albumin, creatinine kinase (creatinine phosphokinase [CPK]), glucose (fasted), Cystatin-C.

Fasting Lipid Panel

- Triglycerides, total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL)
- Non-fasted samples do not contribute.
- Subjects with lipid-modifying agents at baseline excluded.
- Samples post-initiation of a lipid-modifying agent do not contribute. (See Lipid-Modifying Agents section below).

Urinalysis

- Specific gravity, pH, glucose, protein, blood and ketones by dipstick (with microscopic examination if blood or protein is abnormal), urine albumin/creatinine ratio, urine protein/creatinine ratio, urine phosphate.

Other tests

- Plasma HIV-1 RNA
- CD4+ and CD8+ lymphocyte counts (including CD4:CD8 ratio)
- Hepatitis B [HBsAg, anti-HBc, anti-HBs, Hepatitis B virus (HBV) Deoxyribonucleic acid (DNA)]
- Hepatitis C (anti-HCV)
- Prothrombin time/international normalized ratio (PT/INR)
- Rapid Plasma Reagin (RPR)
- Glycated haemoglobin (HbA1c)
- Pregnancy test for women of childbearing potential

- Data not provided in the GSK standard measurement units by the central laboratory will be converted by PPD using GSK's Integrated Data Standards Library (IDSL) standard conversions in the CONV dataset where necessary.
- Additional non-protocol specified laboratory assessments performed at the institution's local laboratory that are databased will be included in the listings. All analyses/ summaries will be based on central and local laboratory assessments only. For multiple results occurring on the same collection date, the following hierarchy will be used to determine the value used for summaries:

  1. For a sample collection date with both a central lab result and a local lab result, select the central lab result.

2. However, if the central lab result isn't evaluable or is missing, select local lab result.
3. Per analysis visit window, select the most relevant result/ info.

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

Growth and Development

- Z-score categories will be used for each growth and development parameter (weight-for-age, height-for-age and BMI-for-age) and summaries will also be provided by gender.
- Full date of birth has not been collected for this study and as a result, z-scores will not be presented for Week 48 reporting. A protocol amendment to retrospectively collect full date of birth is being considered as well as assessment of likely impact if z-scores are calculated using available partial date of birth information. Calculation and presentation of z-scores for Week 96 reporting onwards is planned using one of these two approaches.
- The reference lines on the growth charts are called z-score lines because they are based on z-scores, also known as standard deviation (SD) scores. Z-scores or SD scores are used to describe how far a measurement is from the median. These scores are calculated differently for measurements that are distributed normally and non-normally in the reference population (https://www.who.int/childgrowth/training/module_c_interpreting_indicators.pdf).
- The charts will be compared with the World Health Organisation (WHO) growth charts as follows:
- 5-19 year olds: WHO Child Growth Charts and WHO Reference 2007 Charts, version WHO. (https://www.who.int/growthref/en/)
- For detailed interpretation for each category for growth and development parameter, refer to pages 27 to 40 of the WHO Growth Record. (https://www.who.int/childgrowth/training/girls_growth_record.pdf?ua=1)

Lab Toxicities – DAIDS Grading

Toxicities will be based on the DAIDS grading system, as specified in the protocol. In addition to the toxicity grading provided by the central laboratory, the grading is being applied programmatically for local lab data to account for any missing grading and to ensure consistency. 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 categorized as in Table 12 according to whether they are above or below the midpoint of normal range.

Table 12 Categorization of Select Lab Parameters Relative to Midpoint of Normal Range

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

If multiple post-baseline records exist with identical worst toxicity grades for any subject, the earliest worst post-baseline record will be used.

Lipid-Modifying Agents
• The following ATC codes correspond to lipid-modifying agents: o ATC Level 2: C10 o ATC Level 3: C10A, C10B (if Level 2 is not available) o 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.
Glomerular Filtration Rate (GFR)
• Glomerular filtration rate (GFR) will be estimated by the central laboratory using the Bedside Schwartz equation [Schwartz, 2009]. In addition, GFR will be estimated by the central laboratory using Creatinine Cystatin C-Based CKiD Equation [Schwartz, 2012] at day 1 and when indicated by renal toxicity criteria.
Hepatitis Status
• Hepatitis C status will be determined using antibody (IgM or IgG) and/or HCV RNA assessments performed during screening. If both antibody and virus RNA assessments are available, 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 HBV if they have a positive surface antigen or detectable HBV DNA during screening. Subject with hepatitis B are excluded from the study.
COVID-19 Pandemic
• Where relationship to COVID-19 is included in outputs, this information will be obtained via eCRF data or CTMS reporting of protocol deviations. • For the purpose of presenting a listing of dates of COVID-19 wave pandemic measures per country, GSK's COVIDIMT dataset will be used as recommended by GSK's COVID-19 Study Integrity Team. This dataset will be shared with PPD prior to production and delivery of each reporting effort.

14.6.4. 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. • HIV-1 RNA <50 c/mL or HIV-1 RNA >=50 c/mL within an analysis window (see Section 14.3) is typically determined by the last available 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 HIV-1 RNA <50 c/mL. Depending on the reason for lack of data, the subject will be classified as HIV-1 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 classified as HIV-1 RNA >=50 c/mL.

HIV-1 RNA

- 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 (e.g. COVID impacts), are included in Section 14.8. 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.
- Both central and local laboratory HIV-1 RNA data for a specific sample collection date will be available when a local lab has been used. In this case the central laboratory results will be prioritised over the local lab result for inclusion in summaries and will be the main driver for snapshot outcomes. All laboratory HIV-1 RNA data will be displayed in listings along with the identification of local vs central / used vs unused in the application of the Snapshot algorithm.

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.

Suspected Virologic Withdrawal (SVW)

- A single HIV-1 RNA value as defined by Virologic Non-response or Virologic Rebound (see below).
- Based on the protocol specific conditions outlined in the protocol, derivation of SVW will use nominal visits and unscheduled visits.
- Visit windowing will not be applied.
- Additional guidelines specified in the protocol related to patient management only and will not be taken into account when programmatically identifying SVW.
- Please refer to section 8.1 of the protocol for details of the derivation.

Confirmed Virologic Withdrawal (CVW)

General Considerations

- A second and consecutive HIV-1 RNA value meeting Virologic Non-response or Rebound.
- Based on the protocol specific conditions outlined in the protocol, derivation of 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 8.1) will not be used when programmatically identifying CVW.

HIV-1 RNA

- 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 value. Note: study drug interruptions will not be taken into account when programmatically identifying CVW.
- Additional guidelines specified in the protocol related to patient management only and will not be taken into account when programmatically identifying CVW.
- Please refer to section 8.1 of the protocol for details of the derivation.

There are 3 parts to the derivation of CVW.

Virologic Non-response (Parts 1 & 2)

- A decrease in plasma HIV-1 RNA of less than 1 log10 c/mL at or after Week 12, with subsequent confirmation, unless plasma HIV-1 RNA is <200 c/mL.
- Confirmed plasma HIV-1 RNA levels ≥200 c/mL at or after Week 24.

Virologic Rebound (Part 3)

- Confirmed rebound in plasma HIV-1 RNA levels to ≥200 c/mL after prior confirmed suppression to <200 c/mL.

If the calculation results in both rebound and non-response, it would be reported as a rebound.

Part 1. A decrease in Plasma HIV-1 RNA of less than 1 log10 c/mL only at or after week 12, with subsequent confirmation, unless Plasma HIV-1 RNA is <200 c/mL

- This applies to at or after Week 12 data only (programming note: include unscheduled visits as a part of a confirmation)
- If there is a decrease < 1 log10 from Baseline at or after Week 12 and HIV-1 RNA >=200 c/mL, then -> suspected virologic withdrawal
- If there is a confirmatory sample, then check if there is a decrease <1 log10 from Baseline and the HIV-1 RNA >=200 c/mL then -> confirmed virologic withdrawal
- Example: Part 1, subject PPD – confirmed virologic withdrawal on PPD

Example: Part 1, subject PPD

subject	visit	visit date	c/mL	log10 c/mL	log10 decrease from BL	CV outcome	comments
PPD	Baseline	PPD	3398	3.53			
	Week 4		39	1.59	1.94		
	Week 8		2354	3.37	0.16		
	Week 12		368742	5.56	-2.03	Suspected virologic withdrawal	<1 log 10 decrease from baseline,

HIV-1 RNA

							and value >200 c/mL
PPD	Week 12 retest	PPD	17293	4.24	-0.71	Confirmed virologic withdrawal	<1 log 10 decrease from baseline, and value >200 c/mL

Part 2: Confirmed Plasma HIV-1 RNA levels >=200 c/mL on or after Week 24

- If patient is not already a confirmed VF due to the rules in Part 1, we can then continue to check the results from Week 24 onwards.
- If a patient has a sample on/after Week 24 and the result is >=200 c/mL then -> suspected virologic withdrawal.
- If a patient, then has a 2nd consecutive sample >=200 c/mL then -> confirmed virologic withdrawal.
- Example: Part 2, subject PPD - confirmed virologic withdrawal on PPD

Example: Part 2, subject PPD

subject	visit	visit date	c/mL	log10 c/mL	log10 decrease from BL	CV outcome	comments
PPD	Baseline	PPD	38286	4.58			
	Week 4		332	2.52	2.06		
	Week 8		400	2.60	1.98		
	Week 12		<50	<1.70	2.99		
	Week 24		87394	4.94	-0.36	Suspected virologic withdrawal	value >200 on/after week 24
	Week 24 retest	PPD	213	2.62	1.97	Confirmed virologic withdrawal	Consecutive value >200 on/after week 24

Part 3: Confirmed rebound in plasma HIV-1 RNA levels to >=200 c/mL after prior confirmed suppression to <200 c/mL

- Patient must have 2 consecutive values <200 c/mL, followed at any time (not necessarily immediately) by 2 consecutive values >=200 c/mL.
- Once a patient has 2 consecutive values <200 c/mL, if any following value is >=200 c/mL then -> suspected rebound.
- If a patient, then has a 2nd consecutive sample >=200 c/mL then -> confirmed rebound

HIV-1 RNA

– Example: Part 3, subject PPD - confirmed rebound on PPD

Example: Part 3, subject PPD

subject	visit	visit date	c/mL	log10 c/mL	log10 decrease from BL	CV outcome	comments
PPD	Baseline	PPD	303007	5.48			
	Week 4		170	2.23	3.25		
	Week 8		140	2.15	3.33		
	Week 12		166	2.22	3.26		
	Week 16		29153	4.46	1.02	Suspected rebound	2 consecutive values <200, followed by an initial value >=200
	Week 16 retest		454	2.66	2.82	Confirmed rebound	2nd consecutive sample >=200
	Withdrawal		<40	1.59	3.89		

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 12.6).
- Any 'other' conditions reported in the CRFs 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.
- Note that the CD4+ T-lymphocyte count takes precedence over the CD4+ T-lymphocyte percentage in HIV infection stages 1, 2, and 3. The CD4+ T-lymphocyte percentage should only be considered if the count is missing.

HIV infection, stage 0

Indicates early HIV infection, inferred from a negative or indeterminate HIV test result within 180 days of a positive result. The criteria for stage 0 supersede and are independent of criteria used for other stages.

HIV-1 RNA

HIV infection, stage 1
 	
• Laboratory confirmation of HIV infection with no AIDS-defining condition, and
  o CD4+ T-lymphocyte count of ≥500 cells/µL, or
  o CD4+ T-lymphocyte percentage of total lymphocytes of ≥26%.
 	
HIV infection, stage 2
 	
• Laboratory confirmation of HIV infection with no AIDS-defining condition, and
  o CD4+ T-lymphocyte count of 200 to 499 cells/µL, or
  o CD4+ T-lymphocyte percentage of total lymphocytes of 14% to 25%.
 	
HIV infection, stage 3 (AIDS)
 	
• Laboratory confirmation of HIV infection, and
  o CD4+ T-lymphocyte count of <200 cells/µL, or
  o CD4+ T-lymphocyte percentage of total lymphocytes of <14%, or
  o Documentation of an AIDS-defining condition (see below).
 	
Documentation of an AIDS-defining condition supersedes a CD4+ T-lymphocyte count of >200 cells/µL and a CD4+ T-lymphocyte percentage of total lymphocytes of >14%.
 	
HIV infection, stage unknown
 	
• Laboratory confirmation of HIV infection, and
  o No information on CD4+ T-lymphocyte count or percentage, and
  o No information on presence of AIDS-defining conditions.
 	
Category C-defining opportunistic illnesses in HIV infection
 	
• Candidiasis of bronchi, trachea, or lungs
• Candidiasis of oesophagus
• Cervical cancer, invasive

HIV-1 RNA
• Coccidioidomycosis, disseminated or extrapulmonary • Cryptococcosis, extrapulmonary • Cryptosporidiosis, chronic intestinal (>1 month's duration) • Cytomegalovirus disease (other than liver, spleen, or nodes), onset at age >1 month • Cytomegalovirus retinitis (with loss of vision) • Encephalopathy, HIV-related • Herpes simplex: chronic ulcers (>1 month's duration) or bronchitis, pneumonitis, or oesophagitis (onset at age >1 month) • Histoplasmosis, disseminated or extrapulmonary • Isosporiasis, chronic intestinal (>1 month's duration) • Kaposi's sarcoma • Lymphoma, Burkitt's (or equivalent term) • Lymphoma, immunoblastic (or equivalent term) • Lymphoma, primary, of brain • Mycobacterium avium complex or Mycobacterium kansasii, disseminated or extrapulmonary • Mycobacterium tuberculosis of any site, pulmonary, disseminated or extrapulmonary • Mycobacterium, other species or unidentified species, disseminated or extrapulmonary • Pneumocystis jirovecii pneumonia • Pneumonia, recurrent • Progressive multifocal leukoencephalopathy • Salmonella septicaemia, recurrent • Toxoplasmosis of brain, onset at age >1 month • Wasting syndrome attributed to HIV.

14.6.5. Viral Genotyping and Phenotyping

14.6.5.1. Genotype

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., Q148K/H or Q148K/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.

Table 13 shows how different amino acid changes will be represented.

Table 13 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'

An assessment will be made of every change across all amino acids within the IN encoding region at Day 1 and time of meeting confirmed withdrawal criteria, with particular attention paid to specific amino acid changes associated with the development of resistance to RAL, EVG, BIC or DTG. The known IN mutations associated with the development of resistance to RAL, EVG, BIC or DTG are shown in Table 14.

Table 14 IN Mutations Associated with Development of Resistance to DTG

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

Amino Acids in HIV Integrase for Analysis	H51Y, **T66A/I/K**, **E92Q/V**/G, Q95K, T97A, G118R, **F121Y**, E138A/K /T, G140A/C/S, **Y143C/H/R/K/S/G/A, P145S, Q146P, S147G, Q148H/K/R**/N, **V151L**/A, S153F/Y, **N155H**/S/T, E157Q, G163R/K, S230R, R263K L68V/**I**,* L74**I**/M, * E138D,* V151I,* G193E *

Note: draft listing; may be modified in case of additional substantive data availability.

- INI mutations listed taken from Stanford HIV Resistance Database (https://hivdb.stanford.edu/dr-summary/pattern-scores/INSTI/ cited 10Oct2018) and accessed on 14Nov2018.
- Each INI mutation listed had a score of ≥10. INI substitutions listed above in bold had a score of =60. * Denotes additional INI mutations added as they were identified during in vitro passage of DTG or seen in a previous DTG study in INI-experienced subjects (ING112574).

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.

Table 15 Major Mutations Associated with Resistance to Other Classes

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.

14.6.5.2. Phenotype

Phenotypic susceptibility to all licensed antiretroviral drugs DTG, will be determined using PhenoSense HIV assays from Monogram Inc. and will be reported as fold change (FC) in IC_{50} relative to wild-type control virus NL4-3, i.e., FC of sample virus = IC_{50} of sample virus/IC_{50} 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 as shown in Table 16 (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.

Table 16 Clinical and Biological Cut-off Values for the PhenoSense HIV Drug Resistance Assay

Drug	Abbreviation	Class	PhenoSense cut-off
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 cut-off (lower cut-off – higher cut-off)

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 cut-offs 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).

Table 17 Biological/Clinical Cut-off:

Fold Change	Score	Interpretation
> clinical lower cut-off or biologic cut-off	0	resistance
≤ clinical lower cut-off or biologic cut-off	1	sensitive

Table 18 Clinical Cut-off:

Fold Change	Score	Interpretation
> clinical higher cut-off	0	resistance
≤ clinical higher cut-off and > clinical lower cut-off	0.5	partially sensitive
≤ clinical lower cut-off	1	sensitive

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

14.6.6. 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 randomised to DTG + 3TC), 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 withdraw 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 about cut-off rules 3, 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, 96 and 144 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.

14.6.7. Analysis Datasets

14.6.7.1. Snapshot Algorithm

For all efficacy analysis, each subject's response (i.e., HIV-1 RNA <50 c/mL) will be calculated according to the US Food and Drug Administration (FDA)'s Snapshot algorithm. According to the Snapshot algorithm substitutions in background therapy (in-class or cross-class) permitted per protocol for documented toxicity reasons are allowed only on or before the first trial visit without penalty.

The Snapshot algorithm will treat all subjects without HIV-1 RNA data at the visit of interest (due to missing data or discontinuation of IP prior to visit window) as non-responders, as well as subjects who switch their concomitant Antiretroviral therapy (ART) prior to the visit of interest, since no switches are permitted per protocol (see section 10.2.5). For subjects with HIV-1 RNA data at the visit of interest, HIV-1 RNA <50 c/mL or HIV-1 RNA >=50 c/mL will be determined by the last available HIV-1 RNA assessment while the subject is on-treatment within the visit window of interest (see Appendix 3 Assessment Windows). These are in accordance with the Snapshot algorithm.

Snapshot study outcomes will be repeated in exactly the same way as the standard Snapshot Algorithm using the modified snapshot algorithm. The modified snapshot still reports high-level categories but 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.

Full details on the Snapshot algorithm and the Modified Snapshot algorithm are contained in Appendices 13.8.1 and 13.8.2.

14.6.7.2. Observed Case

The observed case (OC) dataset uses only the data that is available at a particular time point, with no imputation for missing values. This data will be used primarily for safety analyses and for some analyses of efficacy.

14.6.8. CD4+ Cell Counts

CD4+ values provided as non-numeric, censored results from the central laboratory e.g., '<0.02' in original units of GI/L will be imputed as 0.019 and '≤0.02' in original units of GI/L will be imputed as 0.02 so that they are converted to standard units of cells/mm^3 and

included in the CD4 summary statistics. The listing will report the censored result as '<20' in the standard units, i.e., equivalent to <0.02 GI/L.

14.6.9. Pharmacokinetic

- Derived DTG and 3TC plasma PK parameters including, but not limited to area under the concentration-time curve (AUC_{0-tau}), maximum observed concentration (C_{max}), time of maximum observed concentration (t_{max}), C0, C24 and terminal half-life ($t_{½}$).

General

- Data at specific timepoints of subjects who had major PK protocol deviations that could impact DTG or 3TC exposure will be removed, as detailed below:

PK Protocol Deviation	Populations Affected	Analysis Consideration
Use of prohibited medications* at time of sample	- Intensive Pharmacokinetic Population - Sparse + Trough Pharmacokinetic Population	Samples will be excluded from summaries and figures but will be included in listings and flagged

- Listings will be based on intensive and sparse + trough pharmacokinetic populations.
- The intensive pharmacokinetic population will be used for calculating PK parameters, summaries of concentration-time data and plotting of individual concentration-time files for the intensive PK population.
- The sparse + trough pharmacokinetic population will be used for summarizing PK concentrations and plotting of individual concentration-time files for the sparse + trough population.
- * Prohibited medications that could decrease DTG or 3TC exposure will be identified as leading to exclusion from PK summaries and figures if they are ongoing at the visit at which the analysis is taking place. If a prohibited medication has a non-missing start and stop date before, say Week 24, then there will be no exclusion from PK analyses at the Week 24 analysis. Prohibited medications are defined as follows:
    - Carbamazepine
    - Oxcarbamazepine
    - Phenobarbital
    - Phenytoin
    - Rifampin
    - Rifapentine

- St. John's wort.

PK Concentrations and Parameters

How to handle values below the quantification limit for the calculation of individual pharmacokinetic profiles

If one or more non-quantifiable (NQ) values occur in a profile before the first measurable concentration, they will be assigned a value of zero concentration. For linear plots, zero concentration value(s) before the first measurable concentration will be included in the plot. For semi-logarithmic log-linear plots, zero concentration value(s) before the first measurable concentration will be assigned a missing value.

If a single NQ value occurs between measurable concentrations in a profile, the NQ should generally be omitted (set to missing) in the derivation of pharmacokinetic parameters, statistical analysis, and the individual subject plots.

If two or more NQ values occur in succession between measurable concentrations, the profile will be deemed to have terminated at the last measurable concentration prior to these NQs. For the purpose of individual subject plots, these NQs will be set to 0, and the subsequent measurable concentrations will be retained. For the derivation of pharmacokinetic parameters, these NQs and any subsequent measurable concentrations will be omitted (set to missing).

NQs which occur after the last measurable concentration will be omitted (set to missing) in the derivation of pharmacokinetic parameters and from the individual subject plots. In some circumstances, there may be a pharmacokinetic rationale for fluctuation resulting in non-measurable concentrations in the middle of the concentration-time profile (e.g., entero-hepatic recycling, erratic absorption from transdermal/inhaled formulations). In these cases, the NQ values could be set to missing or to some other values (e.g., ½ LLQ) and subsequent valid concentrations may be retained. A reference line indicating LLQ would then be included in plots.

For the calculation of mean or median pharmacokinetic profiles

When estimating the mean or median value for the concentration at a given time point (i.e., descriptive mean or median curve), the following guidelines should be considered: All NQ values will be set to zero except when an individual NQ falls between two quantifiable values, in which case it will be omitted from the calculation of mean or median profiles. Measurable concentrations which follow more than one consecutive mid-profile NQ will be omitted (set to missing).

The mean/median value at a time-point where one or more samples have NQ values will be reported (in tabular or graphical fashion) even if the mean/median value is below the LLQ of the assay. For linear plots, zero concentration value(s) will be included in the plot. For semi-logarithmic log-linear plots, zero concentration value(s) will be assigned a missing value. Zero mean or median values will be included in summary tables.

In certain cases, the NQ values could be set to missing or to some other values (e.g., ½ LLQ) with proper scientific justification(s). A reference line indicating LLQ would then be included in plots.

It should be noted that a high proportion of NQ values may affect the standard deviation (SD); if more than 30% of values are imputed, then SD will not be displayed. Any table of summary statistics for concentration-time data will report N (number of subjects in the analysis population), n (number of subjects with non-missing values) and number imputed (number of subjects with imputed values (i.e., NQ assigned zero concentration). BQL (Below the Quantification Limit) may be displayed in listings by legacy systems instead of NQ; these abbreviations are interchangeable and mean that a sample has been received, analysed and a concentration below the LLQ of the assay found.

Scientific judgement and prior knowledge should always be used in applying these guidelines.

How to Handle Anomalous Concentration Values

Individual concentrations deemed to be anomalous will be excluded from the pharmacokinetic analysis and median and mean profiles; such anomalous values will be identified (e.g., flagged by an asterisk or an appropriate footnote) in the data listings of the study report. Anomalous values are those that are inconsistent with known or expected pharmacokinetic behaviour of the drug, and are not defined in a statistical outlier sense. Clear justification must be provided in the report for exclusion of any data. Individual plasma concentration-time profiles by actual time and median/mean profiles by treatment (dose) by nominal time will be plotted. Each of the figures will contain one plot on the untransformed scale (i.e., a linear plot) and one plot on the loge-transformed scale (i.e., semi-logarithmic log-linear plot). In addition, a plot showing all individual subjects for each treatment (dose) will be produced (both linear and semi-logarithmic log-linear).

Not applicable to analyses post Week 48.

14.6.10. Population Pharmacokinetic (PopPK)

Not applicable to analyses post Week 48. Further details to be included in a separate RAP.

14.7. Appendix 7: Premature Withdrawals & Handling of Missing Data

14.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as if he/she completes 48 weeks of treatment and either completes the follow up visit 4 weeks after Week 48 or continues into the Extension Phase of this study. • A participant will be considered to have completed the Extension Phase if he/she completes the Week 144 visit. • A participant will be considered to have completed the Continuation Phase after completion of the End of Continuation Phase Visit. • Withdrawn subjects were not replaced in the study. • All available data from subjects who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

14.7.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: o 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 is excluded from the table. o Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such.
Methods for Proportion Endpoints Based on Plasma HIV-1 RNA - Snapshot	• For each scheduled assessment time, the Snapshot response rate for a given threshold (e.g., <50 c/mL) is defined as: $\text{Snapshot Rate} = \frac{\text{Number of responders in that analysis window}}{\text{Number of subjects in the analysis population}}$ • In each analysis window, a subject is defined as a responder as per the algorithm described in section 14.6.4 In particular, if no HIV-1 RNA assessment is available for a subject in the assessment window, then that subject will be counted as a non-responder. The nature of this missing data will be further classified in Snapshot summaries as either 'HIV-1 RNA >=50 c/mL' or 'No Virologic Data at Week X'; see section 14.6.4 for full details.

Element	Reporting Detail
Laboratory data (e.g., HIV-1 RNA, CD4+ cell counts, haematology, and clinical chemistry)	• No imputation for missing data or premature discontinuation will be performed and the observed values will be used.

14.7.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: o Missing Start Day: First of the month 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 o : Treatment States and Phases. o Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.
Exposure	If a partial or a missing IP stop date is recorded in the eCRF while study is ongoing, the following convention will be used: • If an IP stop date is partial where the day is missing (i.e., MMMYYYY), the last day of the month (28/29/30/31 depending on the month and year), the date of last visit, or the recorded date of withdrawal/completion, whichever is earlier, will be used. • If an IP stop date is partial where the day and month are missing, the last day of the year i.e., 31DECYYYY, the date of last visit, or the recorded date of withdrawal/completion, whichever is earlier, will be used. • If an IP stop date is completely missing, the date of last visit or the recorded date of withdrawal/completion, whichever is earlier, will be used.
Concomitant Medications	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month

Element	Reporting Detail
	○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) 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.

14.8. Appendix 8: Snapshot and Modified Snapshot Algorithm Details

14.8.1. Snapshot Algorithm Details

Detailed Algorithm Steps		
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/mL [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 participants 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
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, as recorded in eCRF 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 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.

Examples from FDA guidance

Data in Window

Virologic outcome should be determined by the last available measurement while the patient is on treatment and continued on trial within the time window:

- HIV-RNA = 580 c/mL at Day 336, HIV-RNA below 50 c/mL on Day 350. This should be categorized as HIV-RNA below 50 c/mL.

No Data in Window

Discontinued study due to Adverse Event or Death:

- Any patient who discontinues because of an AE or death before the window should be classified as *Discontinued due to AE or Death* (as appropriate), regardless of the HIV-RNA result, even if the HIV-RNA is below 50 c/mL at the time of discontinuation.
- However, if a patient has an HIV-RNA value in the time window and also discontinues in the time window, the viral load data should be used to classify the patient's response. This is the Virology First hierarchy:
    a. HIV-RNA below 50 c/mL at Day 336 and discontinues because of AE or even dies on Day 360 — this person is categorized as having HIV-RNA below 50 c/mL.
    b. HIV-RNA is 552 c/mL on Day 336 and the patient discontinues on Day 360, the patient is categorized as having HIV-RNA greater than or equal to 50 c/mL.

Discontinued for Other Reasons:

- Only patients who have achieved virologic suppression can be counted as *Discontinued for Other Reasons.*
- If a patient discontinues the study before the window because of *lack of efficacy* then the patient should be included in the HIV-RNA greater than or equal to 50 row and not in the Discontinued for Other Reasons row.
- If a patient discontinues because of *subject withdrew consent* and his or her HIV-1 RNA result at the time of discontinuation was equal to or above 50 c/mL, then he or she should be categorized as HIV-RNA greater than or equal to 50 and NOT as Discontinued for Other Reasons.
- If a patient discontinued because of *Lost to Follow-Up* and the last HIV-RNA result was 49 c/mL, then the patient can be categorized as Discontinued for Other Reasons.

- If patients changed background treatment — *not permitted by protocol*— they should be considered an efficacy failure and captured in the HIV-RNA greater than or equal to 50 c/mL row.

On study but missing data in window:

- If there are no data during Days 294 to 377, but there is an HIV-RNA below 50 c/mL on Day 380, this patient should be considered *On Study but Missing Data in Window.*
- If there are no data during Days 294 to 377, but there is an HIV-RNA equal to or above 50 c/mL on Day 280, this patient also should be classified as *On Study but Missing Data in Window.*

Optimized Background Therapy Substitutions After Randomisation

- OBT substitutions (in-class or cross-class) permitted per protocol for documented toxicity reasons can be permitted on or before the first trial visit without penalty.

If OBT substitutions for toxicity reasons occur after the first trial visit, then patients should be categorized as having HIV-RNA greater than or equal to 50 c/mL if they have HIV-RNA above 50 c/mL at the time of switch.

14.8.2. 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 outcome still reports high-level categories (>=50 c/mL, <50 c/mL and No Virologic Data) in exactly the same way as the standard Snapshot Algorithm in Section 14.8.1, however it reports additional subcategories to account for outcomes related to COVID-19.

Condition ('Week 48' indicates Week 48 window)	**Response**	**Reasons**
1.1 If ***non-permitted*** change in background therapy ***prior to*** Week 48 (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 48 (COVID-19 switch)	HIV1-RNA ≥ 50	Change in background therapy (COVID-19 related)

2.1 If ***permitted*** change (not related to COVID-19) in background therapy ***prior to*** Week 48 AND the latest on-treatment VL prior to/on the date of change is ≥ 50 c/mL	HIV1-RNA ≥ 50	Change in background therapy (Non- COVID-19 related)
2.2 If ***permitted*** change (related to COVID-19) in background therapy ***prior to*** Week 48 AND the latest on-treatment VL prior to/on the date of change is ≥ 50 c/mL	HIV1-RNA ≥ 50	Change in background therapy COVID-19 related)
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	
• 3.3.1 No VL during Week 48 prior to/on the date of change (non-COVID-19 related)	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 (COVID-19 related)	HIV1-RNA ≥ 50	Change in background therapy (COVID-19 related)
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]		
4.1.1 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 missed visit not 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 and pandemic-related not equal to 'Yes')		
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, investigator discretion, as recorded in eCRF Study Conclusion Form, and pandemic-related='Yes')		
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 Lack of efficacy	HIV1-RNA ≥ 50	Disc. for lack of efficacy (COVID-19 related)
5.3.2.4.3 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 (COVID-19 related)

Detailed steps

Condition ('Week 48' indicates Week 48 window)	**Response**	**Reasons**
1.1 If ***non-permitted*** change in background therapy ***prior to*** Week 48 (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 48 (COVID-19 switch)	HIV1-RNA ≥ 50	Change in background therapy

		(COVID-19 related)
2.1 If ***permitted*** change (not related to COVID-19) in background therapy ***prior to*** Week 48 AND the latest on-treatment VL prior to/on the date of change is ≥ 50 c/mL	HIV1-RNA ≥ 50	Change in background therapy (Non- COVID-19 related)
2.2 If ***permitted*** change (related to COVID-19) in background therapy ***prior to*** Week 48 AND the latest on-treatment VL prior to/on the date of change is ≥ 50 c/mL	HIV1-RNA ≥ 50	Change in background therapy COVID-19 related)
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	
• 3.3.1 No VL during Week 48 prior to/on the date of change (non-COVID-19 related)	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 (COVID-19 related)	HIV1-RNA ≥ 50	Change in background therapy (COVID-19 related)
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]		
4.1.1 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 missed visit not 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 and pandemic-related not equal to 'Yes')		
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, investigator discretion, as recorded in eCRF Study Conclusion Form, and pandemic-related='Yes')		
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 Lack of efficacy	HIV1-RNA ≥ 50	Disc. for lack of efficacy (COVID-19 related)
5.3.2.4.3 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 (COVID-19 related)

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

14.9. Appendix 9: Abnormalities of Potential Clinical Concern

14.9.1. Abnormalities of Potential Clinical Concern

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 of potential clinical concern/importance will be defined as any Grade1-5 toxicity.

14.10. Appendix 10 – Abbreviations & Trademark

14.10.1. Abbreviations

Abbreviation	Description
3TC	Lamivudine, EPIVIR
λ_z	Apparent terminal rate constant
ABC	Abacavir, ZIAGEN
ADaM	Analysis Data Model
AE	Adverse Event
AIDS	Acquired immunodeficiency syndrome
ALP	alkaline phosphatase
ALT	Alanine aminotransferase
Anti-HBc	Hepatitis B core antibody
Anti-HBs	Hepatitis B surface antibody
ART	Antiretroviral therapy
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
ATV	Atazanavir
AUC	Area under the concentration-time curve
AUC(0-τ)	Area under the concentration-time curve over the dosing interval
AZT (ZDV)	Zidovudine
BIC	bictegravir
BUN	blood urea nitrogen
C_0	Observed pre-dose concentration

Abbreviation	Description
C_{24}	Concentration in the plasma at 24 hours after dosing
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
C_{max}	Maximum observed concentration in plasma (ng/mL), determined directly from the concentration-time data.
c/mL	Copies/mL
CRF	Case report form
CSR	Clinical Study Report
CTMS	Clinical Trial Management System
CVW	Confirmed virologic withdrawal
d4T	Stavudine
DAIDS	Division of Acquired Immunodeficiency Syndrome
ddI	Didanosine
DLV	Delavirdine
DNA	Deoxyribonucleic acid
DOV	Date of Visit
DP	Decimal Places
DRV	Darunavir
DTG	Dolutegravir, TIVICAY
eCRF	Electronic Case Record Form
eC-SSRS	electronic Columbia Suicidality Severity Rating Scale

Abbreviation	Description
EFV	Efavirenz
ELV	Elvitegravir
ETR	Etravirine
FDA	Food and Drug Administration
FDC	Fixed-dose combination
FTC	Emtricitabine
FPV	Fosamprenavir
GSK	GlaxoSmithKline
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HDL	high density lipoprotein
HIV	Human immunodeficiency virus
ICH	International Conference on Harmonisation
IDSL	Integrated Data Standards Library
IDV	Indinavir
IN	Integrase
INI	Integrase (inhibitor)
INR	International normalized ratio
INSTI	Integrase strand transfer inhibitor
IP	Investigational Product
ITT	Intent-To-Treat
LDL	low density lipoprotein

Abbreviation	Description
LMA	Lipid modifying agent
LPV	Lopinavir
MCH	mean cell hemoglobin
MCV	mean corpuscle volume
MedDRA	Medical Dictionary for Regulatory Activities
MUERC	Maseno University Ethics Review Committee
NCEP	National Cholesterol Education Program
NFV	Nelfinavir
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NVP	Nevirapine
OC	Observed Case
PD	Protocol Deviation
PI	Protease inhibitor
PK	Pharmacokinetic
PP	Per Protocol
PPD	Pharmaceutical Product Development
PR	Protease
RAL	Raltegravir
RAP	Reporting and analysis plan
RBC	red blood cell
RNA	Ribonucleic acid

Abbreviation	Description
RPR	Rapid Plasma Reagin
RPV	Rilpivirine
RT	Reverse transcriptase
SAE	Serious adverse event
SDTM	Study Data Tabulation Model
SDV	Source data verification
SOC	System Organ Class
SOP	Standard Operation Procedure
SQV	Saquinavir
SVW	Suspected virologic withdrawal
$t_{½}$	Apparent terminal half-life
TDF	Tenofovir
t_{max}	Time to reach C_{max}
TPV	Tipranavir
TRDF	Treatment-Related Discontinuation = Failure
ULN	Upper limit of normal
WBC	white blood cell
WHO	World Health Organization
ZDV	Zidovudine, RETROVIR
ZDV/3TC	Zidovudine/lamivudine, COMBIVIR

14.10.2. Trademark

Trademark of ViiV Healthcare
EPIVIR

Trademark not owned by ViiV Healthcare
Atripla

Trademark of ViiV Healthcare
EPZICOM
KIVEXA
TIVICAY
TRIZIVIR
COMBIVIR

Trademark not owned by ViiV Healthcare
Complera
Emtriva
Efavirenz
GeneXpert
GenoSure
Isentress
MedDRA
Monogram Biosciences
PhenoSense
Quest Diagnostics
SAS
WinNonlin

14.11. Appendix 11 - List of Data Displays

14.11.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.27	
Efficacy	2.1 to 2.13	2.1 to 2.5
Safety	3.1 to 3.36	3.1 to 3.2
Virology	4.1 to 4.9	
Pharmacokinetic	5.1 to 5.6	5.1 to 5.8
Section	**Listings**	
ICH Listings	1 to 25	
Other Listings	26 to 66	

14.11.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 14.11.

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
Virology	VIRAL_Fn	VIRAL_Tn	VIRAL_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 'IDSL / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

14.11.3. Deliverables

Delivery	Description
IDMC SAC	IDMC Statistical Analysis Complete
Week 48 SAC	Statistical Analysis Complete at Week 48
Week 96 SAC	Statistical Analysis Complete at Week 96
Week 144 SAC	Statistical Analysis Complete at Week 144
Study Conclusion	Final Study Conclusion Analysis Complete

14.12. Appendix 12: Table of Contents

14.12.1. Table of Contents

14.12.1.1. Study Population

The ITT-E Population will be used, except where noted.

14.12.1.1.1. Tables

Number	Title	Details/ Comments	Reports	IDSL/ TST ID / Example Shell
1.1	Summary of Study Populations	Based on the 'All Subjects Screened Population'. Report for IDMC contains: All Subjects Screened, Enrolled, Safety, ITT-E, PP, CVW, PK, Sparse PK and Intensive PK populations. Report for Week 48 contains all of the above (excluding Sparse PK), additionally with: Sparse + Trough PK population, Safety Sens 1, Safety Sens 2, ITT-E EP, ITT-E Sens 1, ITT-E Sens 2, ITT-E EP Sens 1 and ITT-E EP Sens 2. Reports for Weeks 96 and 144 contain all populations described in Section 5.1 and Enrolled subjects.	IDMC Week 48 Week 96 Week 144	SP1
1.2	Summary of Subjects by Country and Investigator	All Subjects Screened Population	Week 48 Week 96 Week 144	NS1
1.3	Summary of Screening Status and Reasons for Screen Failure	All Subjects Screened Population	Week 48 Week 96 Week 144	ES6
1.4	Summary of Number of Subjects Attending Nominal and Actual Analysis Visits		Week 48 Week 96 Week 144	POP_T1

Number	Title	Details/ Comments	Reports	IDSL/ TST ID / Example Shell
1.5	Summary of Recruitment by Country and Site Before & After Implementation of Pandemic Measures	All Subjects Screened Population	Week 48 Week 96 Week 144	NS1
1.6	Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Study Conclusion Record	Present by "Not Related to COVID-19" and " Related to COVID-19" and Overall , Study conclusion (after last subject leaves the study)	Week 48 Week 96 Week 144	ES1
1.7	Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Treatment Phase Conclusion Record	Present by "Not Related to COVID-19" and " Related to COVID-19" and Overall	IDMC Week 48 Week 96 Week 144	ES1
1.8	Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Extension Phase Conclusion Record	Based on the ITT-E EP population. Present by "Not Related to COVID-19" and " Related to COVID-19" and Overall	Week 48 Week 96 Week 144	ES1
1.9	Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Continuation Phase Conclusion Record	Present by "Not Related to COVID-19" and " Related to COVID-19" and Overall	Week 96 Week 144	ES1
1.10	Summary of Reasons for Withdrawal by Visit		Week 48 Week 96 Week 144	POP_T2
1.11	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment by Relationship to COVID-19 Pandemic	Present by "Not Related to COVID-19" and " Related to COVID-19" and Overall	Week 48 Week 96 Week 144	SD1
1.12	Summary of Important Protocol Deviations by Relationship to COVID-19	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week	Week 48 Week 96 Week 144	DV1

Number	Title	Details/ Comments	Reports	IDSL/ TST ID / Example Shell
		96 or Week 144 info, as relevant. Present by "Not Related to COVID-19" and " Related to COVID-19" and Overall.		
1.13	Summary of Protocol Deviations Leading to Exclusion from the Per-Protocol Population		Week 48	POP_T3
1.14	Summary of Demographic Characteristics		IDMC Week 48 Week 96 Week 144	POP_T4
1.15	Summary of Race and Racial Combinations Details		Week 48 Week 96 Week 144	DM6
1.16	Summary of Hepatitis Status at Entry		Week 48 Week 96 Week 144	POP_T5
1.17	Summary of CDC Classification of HIV Infection at Baseline		Week 48 Week 96 Week 144	CDC1
1.18	Summary of HIV Risk Factors		Week 48 Week 96 Week 144	RF1
1.19	Distribution of Quantitative Plasma HIV-1 RNA (c/mL) Results at Screening and Baseline		IDMC Week 48 Week 96 Week 144	POP_T6
1.20	Distribution of CD4+ Cell Count (cells/mm^3) Results at Screening and Baseline		Week 48 Week 96 Week 144	POP_T7
1.21	Summary of Current Medical Conditions at Screening		Week 48 Week 96 Week 144	MH1
1.22	Summary of Past Medical Conditions at Screening		Week 48 Week 96 Week 144	MH1
1.23	Summary of Current Cardiac, Gastrointestinal, Metabolism		Week 48 Week 96	POP_T8

Number	Title	Details/ Comments	Reports	IDSL/ TST ID / Example Shell
	and Nutrition, Psychiatric, Renal and Urinary, and Nervous System Conditions		Week 144	
1.24	Summary of Past Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, and Nervous System Conditions		Week 48 Week 96 Week 144	POP_T8
1.25	Summary of Concomitant Medication by Ingredient ATC Level 1		Week 48 Week 96 Week 144	CM1
1.26	Summary of Concomitant Medication Ingredient Combinations		Week 48 Week 96 Week 144	CM8
1.27	Summary of Concomitant Medication by Combination Term ATC Level 1		Week 48 Week 96 Week 144	CM1
1.28	Sensitivity Analyses 1: Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Study Conclusion Record	Repeat of Table 1.6 on ITT-E Sens 1 population	Week 48 Week 96 Week 144	ES1
1.29	Sensitivity Analyses 2: Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Study Conclusion Record	Repeat of Table 1.6 on ITT-E Sens 2 population	Week 48 Week 96 Week 144	ES1
1.30	Sensitivity Analyses 1: Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Treatment Phase Conclusion Record	Repeat of Table 1.7 on ITT-E Sens 1 population	Week 48 Week 96 Week 144	ES1
1.31	Sensitivity Analyses 2: Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Treatment Phase Conclusion Record	Repeat of Table 1.7 on ITT-E Sens 2 population	Week 48 Week 96 Week 144	ES1

Number	Title	Details/ Comments	Reports	IDSL/ TST ID / Example Shell
1.32	Sensitivity Analyses 1: Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Extension Phase Conclusion Record	Repeat of Table 1.8 on ITT-E EP Sens 1 population	Week 48 Week 96 Week 144	ES1
1.33	Sensitivity Analyses 2: Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic: Extension Phase Conclusion Record	Repeat of Table 1.8 on ITT-E EP Sens 2 population	Week 48 Week 96 Week 144	ES1
1.36	Sensitivity Analyses 1: Summary of Demographic Characteristics	Repeat of Table 1.14 on ITT-E Sens 1 population	Week 48 Week 96 Week 144	POP_T4
1.37	Sensitivity Analyses 2: Summary of Demographic Characteristics	Repeat of Table 1.14 on ITT-E Sens 2 population	Week 48 Week 96 Week 144	POP_T4
1.38	Sensitivity Analyses 1: Distribution of Quantitative Plasma HIV-1 RNA (c/mL) Results at Screening and Baseline	Repeat of Table 1.19 on ITT-E Sens 1 population	Week 48 Week 96 Week 144	POP_T6
1.39	Sensitivity Analyses 2: Distribution of Quantitative Plasma HIV-1 RNA (c/mL) Results at Screening and Baseline	Repeat of Table 1.19 on ITT-E Sens 2 population	Week 48 Week 96 Week 144	POP_T6
1.40	Sensitivity Analyses 1: Distribution of CD4+ Cell Count (cells/mm^3) Results at Screening and Baseline	Repeat of Table 1.20 on ITT-E Sens 1 population	Week 48 Week 96 Week 144	POP_T7
1.41	Sensitivity Analyses 2: Distribution of CD4+ Cell Count (cells/mm^3) Results at Screening and Baseline	Repeat of Table 1.20 on ITT-E Sens 2 population	Week 48 Week 96 Week 144	POP_T7

14.12.1.1.2. ICH Listings

Number	Title	Details/ Comments	Reports	IDSL/ TST ID / Example Shell
1	Listing of Screen Failures	All Subjects Screened Population	Week 48 Week 96 Week 144	ES7
2	Listing of Study Conclusion Record Reasons for Study Withdrawal		IDMC Week 48 Week 96 Week 144	ES2
3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		Week 48 Week 96 Week 144	IE3
4	Listing of Important Protocol Deviations		Week 48 Week 96 Week 144	DV2
5	Listing of Protocol Deviations Leading to Exclusion from the Per-Protocol Population		Week 48 Week 96 Week 144	POP_L1
6	Listing of Demographic Characteristics		Week 48 Week 96 Week 144	DM2
7	Listing of Race		Week 48 Week 96 Week 144	DM9
8	Listing of Reasons for Study Treatment Discontinuation		Week 48 Week 96 Week 144	SD2

14.12.1.1.3. Other Listings

Number	Title	Details/Comments	Reports	IDSL/TST ID/ Example Shell
26	Listing of Study Populations	All Subjects Screened Population	Week 48 Week 96 Week 144	POP_L2
27	Listing of Subject Recruitment by Country and Site Number	All Subjects Screened Population	Week 48 Week 96 Week 144	POP_L3
28	Listing of Country Level Dates of Waves of COVID-19 Pandemic Measures	All Subjects Screened Population	Week 48 Week 96 Week 144	PAN5A
29	Listing of Protocol Deviations Related to COVID-19	To include columns for 'PDs requiring exclusion from the Per-Protocol Population', 'Important PD Week 24 Cut-Off', and 'Important PD Week 48 Cut-Off'.	Week 48 Week 96 Week 144	DV2
30	Listing of Hepatitis Test Results		Week 48 Week 96 Week 144	POP_L4
31	Listing of CDC Classification of HIV Infection at Baseline		Week 48 Week 96 Week 144	CDC3
32	Listing of HIV Risk Factors		Week 48 Week 96 Week 144	RF2
33	Listing of Current and Past Medical Conditions		Week 48 Week 96 Week 144	MH2
34	Listing of Cardiovascular Risk Assessment Data at Day 1		Week 48 Week 96 Week 144	POP_L5
35	Listing of Investigational Product Accountability		Week 48 Week 96 Week 144	POP_L6
36	Listing of Prior, Concomitant, and Post-treatment Medications		Week 48 Week 96 Week 144	CM3

Number	Title	Details/Comments	Reports	IDSL/TST ID/ Example Shell
37	Listing of Prior Antiretroviral Therapy Stopped Prior to Screening		Week 48 Week 96 Week 144	CM3
38	Listing of Concomitant and Post-Treatment Antiretroviral Therapy	to include sufficient info in the listing to be able to distinguish concomitant and Post-treatment therapy.	Week 48 Week 96 Week 144	CM3

14.12.1.2. Efficacy

The ITT-E Population will be used, except where noted.

14.12.1.2.1. Tables

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
2.1	Summary of Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL – Snapshot Analysis	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	EFF_T1
2.2	Summary of Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 – Snapshot Analysis	Per-Protocol Population.	Week 48	EFF_T1
2.3	Summary of Proportion of Subjects with Plasma HIV-1 RNA <200 c/mL – Snapshot Analysis	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	EFF_T1
2.4	Summary of Study Outcomes (<50 c/mL) – Snapshot Analysis	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	EFF_T2
2.5	Summary of Study Outcomes (<50 c/mL) at Week 48 – Snapshot Analysis	Per-Protocol Population.	Week 48	EFF_T2
2.6	Summary of Study Outcomes (<50 c/mL) – Modified Snapshot Analysis	Week 48 reporting will include separate summaries of Week 24 and 48 info.	Week 48 Week 96 Week 144	EFF_T3

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
		Subsequent reporting will present only Week 96 or Week 144 info, as relevant.		
2.7	Summary of Study Outcomes (<200 c/mL) – Snapshot Analysis	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	EFF_T2
2.8	Summary of Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL by Visit – Snapshot Analysis	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	EFF_T4
2.9	Summary of Proportion of Subjects with Plasma HIV-1 RNA < 200 c/mL by Visit – Snapshot Analysis	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	EFF_T4
2.10	Cumulative Proportion of Subjects Meeting Confirmed Virologic Withdrawal Criteria by Visit		IDMC Week 48 Week 96 Week 144	EFF_T5
2.11	Distribution of Quantitative Plasma HIV-1 RNA Results at Time of Meeting Suspected and Confirmed of Virologic Withdrawal Criteria		IDMC Week 48 Week 96 Week 144	EFF_T6
2.12	Summary of Change from Baseline in Plasma HIV-1 RNA (log10 c/mL) by Visit		IDMC Week 48 Week 96 Week 144	EFF_T7

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
2.13	Summary of Change from Baseline in CD4+, CD8+ Cell Count and Ratio (cells/mm^3) by Visit		Week 48 Week 96 Week 144	EFF_T8
2.14	Sensitivity Analyses 1: Summary of Study Outcomes (<50 c/mL) at Week 48 – Snapshot Analysis	Repeat of Table 2.4 on ITT-E Sens 1 population	Week 48	EFF_T2
2.15	Sensitivity Analyses 2: Summary of Study Outcomes (<50 c/mL) at Week 48 – Snapshot Analysis	Repeat of Table 2.4 on ITT-E Sens 2 population	Week 48	EFF_T2
2.16	Sensitivity Analyses 1: Summary of Study Outcomes (<200 c/mL) – Snapshot Analysis	Repeat of Table 2.7 on ITT-E Sens 1 population	Week 48 Week 96 Week 144	EFF_T2
2.17	Sensitivity Analyses 2: Summary of Study Outcomes (<200 c/mL) – Snapshot Analysis	Repeat of Table 2.7 on ITT-E Sens 2 population	Week 48 Week 96 Week 144	EFF_T2
2.18	Sensitivity Analyses 1: Summary of Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL by Visit – Snapshot Analysis	Repeat of Table 2.8 on ITT-E Sens 1 population	Week 48 Week 96 Week 144	EFF_T4
2.19	Sensitivity Analyses 2: Summary of Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL by Visit – Snapshot Analysis	Repeat of Table 2.8 on ITT-E Sens 2 population	Week 48 Week 96 Week 144	EFF_T4
2.20	Sensitivity Analyses 1: Summary of Proportion of Subjects with Plasma HIV-1 RNA < 200 c/mL by Visit –Snapshot Analysis	Repeat of Table 2.9 on ITT-E Sens 1 population	Week 48 Week 96 Week 144	EFF_T4
2.21	Sensitivity Analyses 2: Summary of Proportion of Subjects with Plasma HIV-1 RNA < 200 c/mL by Visit –Snapshot Analysis	Repeat of Table 2.9 on ITT-E Sens 2 population	Week 48 Week 96 Week 144	EFF_T4
2.22	Sensitivity Analyses 1: Summary of Change from Baseline in CD4+, CD8+ Cell Count and Ratio (cells/mm^3) by Visit	Repeat of Table 2.13 on ITT-E Sens 1 population	Week 48 Week 96 Week 144	EFF_T8
2.23	Sensitivity Analyses 2: Summary of Change from Baseline in	Repeat of Table 2.13 on ITT-E Sens 2 population	Week 48 Week 96 Week 144	EFF_T8

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
	CD4+, CD8+ Cell Count and Ratio (cells/mm^3) by Visit			

14.12.1.2.2. Figures

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
2.1	Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL by Visit – Snapshot Algorithm	Line plot	Week 48 Week 96 Week 144	EFF_F1
2.2	Proportion (95% CI) of Subjects with HIV-1 RNA <200 c/mL by Visit – Snapshot Algorithm	Line plot	Week 48 Week 96 Week 144	EFF_F1
2.3	Unadjusted Mean (95% CI) Change From Baseline in CD4+ Cell Count (cells/mm^3) by Visit	Line plot	Week 48 Week 96 Week 144	EFF_F2
2.4	Individual Plasma HIV-1 RNA and CD4+ Profiles by Visit for subjects with at least one CVW visit		Week 48 Week 96 Week 144	EFF_F3
2.5	Individual CD8+ and Ratio Profiles by Visit for subjects with at least one CVW visit		Week 48 Week 96 Week 144	EFF_F3
2.6	Sensitivity Analyses 1: Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL by Visit – Snapshot Algorithm	Repeat of Figure 2.1 on ITT-E Sens 1 population	Week 48 Week 96 Week 144	EFF_F1
2.7	Sensitivity Analyses 2: Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL by Visit – Snapshot Algorithm	Repeat of Figure 2.1 on ITT-E Sens 2 population	Week 48 Week 96 Week 144	EFF_F1
2.8	Sensitivity Analyses 1: Proportion (95% CI) of Subjects with HIV-1 RNA <200 c/mL by Visit – Snapshot Algorithm	Repeat of Figure 2.2 on ITT-E Sens 1 population	Week 48 Week 96 Week 144	EFF_F1
2.9	Sensitivity Analyses 2: Proportion (95% CI) of Subjects with HIV-1 RNA <200 c/mL by Visit – Snapshot Algorithm	Repeat of Figure 2.2 on ITT-E Sens 2 population	Week 48 Week 96 Week 144	EFF_F1

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
2.10	Sensitivity Analyses 1: Unadjusted Mean (95% CI) Change From Baseline in CD4+ Cell Count (cells/mm^3) by Visit	Repeat of Figure 2.3 on ITT-E Sens 1 population	Week 48 Week 96 Week 144	EFF_F2
2.11	Sensitivity Analyses 2: Unadjusted Mean (95% CI) Change From Baseline in CD4+ Cell Count (cells/mm^3) by Visit	Repeat of Figure 2.3 on ITT-E Sens 2 population	Week 48 Week 96 Week 144	EFF_F2

14.12.1.2.3. ICH Listings

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
9	Listing of Quantitative and Qualitative Plasma HIV-1 RNA Data	To include TND	IDMC Week 48 Week 96 Week 144	EFF_L1
10	Listing of Study Outcome (<50 c/mL) – Modified Snapshot Analysis	COVID-19 relationship status will be included. Week 24 and 48 reporting will both be included and will be distinguishable by the 'analysis window' column. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	EFF_L2
11	Listing of Study Outcome (<200 c/mL) – Modified Snapshot Analysis	COVID-19 relationship status will be included. Week	Week 48 Week 96 Week 144	EFF_L2

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
		24 and 48 reporting will both be included and will be distinguishable by the 'analysis window' column. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.		

14.12.1.2.4. Other Listings

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
39	Listing of CD4+, CD8+ Cell Count and Ratio Data		Week 48 Week 96 Week 144	Shell
40	Listing of Stage 3 HIV-1 Associated Conditions		Week 48 Week 96 Week 144	HIV4
41	Listing of Plasma HIV-1 RNA for Subjects with Confirmed Virologic Withdrawal	To include TND	IDMC Week 48 Week 96 Week 144	VF4

14.12.1.3. Safety

The Safety Population will be used, except where noted.

14.12.1.3.1. Tables

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
3.1	Summary of Extent of Exposure to Investigational Product		IDMC Week 48 Week 96 Week 144	EX1
3.2	Summary of All Adverse Events by System Organ Class and Preferred Term	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	AE1
3.3	Summary of All Adverse Events by Maximum Toxicity	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	AE5A
3.4	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term		IDMC	AE1
3.5	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term	Week 48 reporting will include	Week 48 Week 96 Week 144	AE1

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
		separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.		
3.6	Summary of Drug-Related Toxicity Grade [redacted] Adverse Events by Frequency	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	AE3
3.7	Summary of Drug-Related Adverse Events by Maximum Toxicity	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	AE5A
3.8	Summary of Adverse Events Experienced by >=2 Subjects by Frequency	Week 48 reporting will include separate summaries of Week 24 and	Week 48 Week 96 Week 144	AE3

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
		48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.		
3.9	Summary of Toxicity Grade CCI Adverse Events by Frequency	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	AE3
3.10	Summary of Common (>=5%) Non-Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	AE15
3.11	Summary of Cumulative Adverse Events and Treatment-Related Adverse Events by Visit		Week 48 Week 96 Week 144	SAFE_T1
3.12	Summary of Serious Adverse Events by System Organ Class and Preferred Term		IDMC	AE1

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
3.13	Summary of Serious Adverse Events by System Organ Class and Preferred Term	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	AE1
3.14	Summary of Drug-Related Serious Adverse Events by System Organ Class and Preferred Term	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	AE1
3.15	Summary of Serious Fatal and Non-Fatal Drug-Related Adverse Events by Overall Frequency	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	AE20
3.16	Summary of Adverse Events Leading to Withdrawal from		IDMC	AE1

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
	Study/Permanent Discontinuation of Study Treatment			
3.17	Summary of Adverse Events Leading to Withdrawal from Study/Permanent Discontinuation of Study Treatment	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	AE1
3.18	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	AE16
3.19	Summary of Chemistry by Visit at or prior to Week X		Week 48 Week 96 Week 144	LB1
3.20	Summary of Chemistry Changes from Baseline by Visit at or prior to Week X		Week 48 Week 96 Week 144	LB1
3.21	Summary of Fasting Lipids by Visit at or prior to Week X		Week 48 Week 96 Week 144	LB1
3.22	Summary of Fasting Lipids Changes from Baseline by Visit at or prior to Week X		Week 48 Week 96 Week 144	LB1
3.23	Summary of Hematology by Visit at or prior to Week X		Week 48 Week 96	LB1

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
			Week 144	
3.24	Summary of Hematology Changes from Baseline by Visit at or prior to Week X		Week 48 Week 96 Week 144	LB1
3.25	Summary of Urinalysis by Visit at or prior to Week X		Week 48 Week 96 Week 144	LB1
3.26	Summary of Urinalysis Changes from Baseline by Visit at or prior to Week X		Week 48 Week 96 Week 144	LB1
3.27	Summary of Maximum Post-Baseline Emergent Chemistry Toxicities	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	SAFE_T2
3.28	Summary of Maximum Post-Baseline Emergent Hematology Toxicities	Week 48 reporting will include separate summaries of Week 24 and 48 info. Subsequent reporting will present only Week 96 or Week 144 info, as relevant.	Week 48 Week 96 Week 144	SAFE_T2
3.29	Summary of True Positive Suicidal Alerts Based on CSSRS by Visit		Week 48 Week 96 Week 144	SAFE_T3
3.30	Summary of Subjects with CSSRS Suicidal Ideation or Behavior at Baseline by Timepoint		Week 48 Week 96 Week 144	SAFE_T4

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
3.31	Summary of Subjects with Post-Baseline CSSRS Suicidal Ideation or Behavior		Week 48 Week 96 Week 144	SAFE_T5
3.32	Summary of Tanner Staging Score by Visit at or prior to Week X		Week 48 Week 96 Week 144	SAFE_T6
3.33	Summary of Tanner Staging Score Changes from Baseline by Visit at or prior to Week X		Week 48 Week 96 Week 144	SAFE_T7
3.34	Summary of Height, Weight and BMI Z-Scores by Visit at or prior to Week X		Week 96 Week 144	SAFE_T8
3.35	Summary of Height, Weight and BMI Z-Score Changes from Baseline by Visit at or prior to Week X		Week 96 Week 144	SAFE_T9
3.36	Summary of COVID-19 Assessments for Subjects with Suspected, Probable or Confirmed COVID-19 Case Diagnosis		Week 48 Week 96 Week 144	PAN1
3.37	Sensitivity Analyses 1: Summary of Extent of Exposure to Investigational Product	Repeat of Table 3.1 on Safety Sens 1	Week 48 Week 96 Week 144	EX1
3.38	Sensitivity Analyses 2: Summary of Extent of Exposure to Investigational Product	Repeat of Table 3.1 on Safety Sens 2	Week 48 Week 96 Week 144	EX1
3.39	Sensitivity Analyses 1: Summary of All Adverse Events by Maximum Toxicity	Repeat of Table 3.3 on Safety Sens 1	Week 48 Week 96 Week 144	AE5A
3.40	Sensitivity Analyses 2: Summary of All Adverse Events by Maximum Toxicity	Repeat of Table 3.3 on Safety Sens 2	Week 48 Week 96 Week 144	AE5A
3.41	Sensitivity Analyses 1: Summary of Drug-Related Adverse Events by Maximum Toxicity	Repeat of Table 3.7 on Safety Sens 1	Week 48 Week 96 Week 144	AE5A
3.42	Sensitivity Analyses 2: Summary of Drug-Related Adverse Events by Maximum Toxicity	Repeat of Table 3.7 on Safety Sens 2	Week 48 Week 96 Week 144	AE5A

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
3.43	Sensitivity Analyses 1: Summary of Serious Adverse Events by System Organ Class and Preferred Term	Repeat of Table 3.13 on Safety Sens 1	Week 48 Week 96 Week 144	AE1
3.44	Sensitivity Analyses 2: Summary of Serious Adverse Events by System Organ Class and Preferred Term	Repeat of Table 3.13 on Safety Sens 2	Week 48 Week 96 Week 144	AE1
3.45	Sensitivity Analyses 1: Summary of Adverse Events Leading to Withdrawal from Study/Permanent Discontinuation of Study Treatment	Repeat of Table 3.17 on Safety Sens 1	Week 48 Week 96 Week 144	AE1
3.46	Sensitivity Analyses 2: Summary of Adverse Events Leading to Withdrawal from Study/Permanent Discontinuation of Study Treatment	Repeat of Table 3.17 on Safety Sens 2	Week 48 Week 96 Week 144	AE1

14.12.1.3.2. Figures

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
3.1	Scatter Plot of Maximum Post-Baseline vs. Baseline for Alanine Aminotransferase (ALT)		Week 48 Week 96 Week 144	LIVER14
3.2	Scatter Plot of Maximum Post-Baseline Alanine Aminotransferase (ALT) vs. Maximum Post-Baseline Total Bilirubin		Week 48 Week 96 Week 144	LIVER9
3.3	Line Plot of Median (IQR) Serum Creatinine & eGFR Over Time		Week 48 Week 96 Week 144	SAFE_F1

14.12.1.3.3. ICH Listings

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
12	Listing of Investigational Product Exposure Data		IDMC Week 48 Week 96	HIV_IP5/ EX3

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
			Week 144	
13	Listing of Investigational Product Dispensed Data		IDMC Week 48 Week 96 Week 144	HIV_IP5/ EX3
14	Listing of All Adverse Events		IDMC Week 48 Week 96 Week 144	AE8
15	Listing of Reasons for Considering as a Serious Adverse Event		Week 48 Week 96 Week 144	AE14
16	Listing of Adverse Events Leading to Withdrawal from Study/Permanent Discontinuation of Study Treatment		IDMC Week 48 Week 96 Week 144	AE8
17	Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Sections 1-2)		Week 48 Week 96 Week 144	PSRAE1
18	Listing of Possible Suicidality-Related Adverse Event Data: Possible Cause(s) (Section 3)		Week 48 Week 96 Week 144	PSRAE3
19	Listing of Possible Suicidality-Related Adverse Event Data (Section 4)		Week 48 Week 96 Week 144	PSRAE4
20	Listing of Possible Suicidality-Related Adverse Event Data (Sections 5-8)		Week 48 Week 96 Week 144	PSRAE5
21	Listing of Subject Numbers for Individual Adverse Events		Week 48 Week 96 Week 144	AE7
22	Listing of Relationship of Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text		Week 48 Week 96 Week 144	AE2
23	Listing of Clinical Chemistry Laboratory Data for Subjects with Laboratory Abnormalities of Potential Clinical Concern		Week 48 Week 96 Week 144	LB5
24	Listing of Hematology Laboratory Data for Subjects with Laboratory		Week 48 Week 96 Week 144	LB5

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
	Abnormalities of Potential Clinical Concern			
25	Listing of Urinalysis Data for Subjects with Abnormalities of Potential Clinical Concern		Week 48 Week 96 Week 144	UR2a

14.12.1.3.4. Other Listings

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
42	Listing of ECG Findings		Week 48 Week 96 Week 144	EG3
43	Listing of Vital Signs – Including Height, Weight and BMI	Z-scores for Week 48 will not be displayed but will be considered for subsequent analysis timepoints.	Week 48 Week 96 Week 144	VS4
44	Listing of Post Baseline Maximum ALT and Maximum Bilirubin		Week 48 Week 96 Week 144	SAFE_L1
45	Subjects Meeting Hepatobiliary Abnormality Criteria - Post-Baseline Emergent		Week 48 Week 96 Week 144	SAFE_L2
46	Listing of CSSRS Suicidal Ideation and Behaviour Data Alerts (4-9)		Week 48 Week 96 Week 144	SAFE_L3
47	Listing of CSSRS Suicidal Ideation and Behaviour Data		Week 48 Week 96 Week 144	SAFE_L4
48	Listing of CSSRS False Positive Alerts with Corresponding Reasons		Week 48 Week 96 Week 144	SAFE_L5
49	Listing of all C-SSRS True Positives, with Corresponding		Week 48 Week 96	SAFE_L6

	Reasons for not being considered an AE or SAE		Week 144	
50	Listing of Subjects Who Became Pregnant During the Study		Week 48 Week 96 Week 144	PREG1a
51	Listing of Tanner Staging Score		Week 48 Week 96 Week 144	SAFE_L7
52	Patient profiles for subjects meeting confirmed virologic withdrawal criteria		Week 48 Week 96 Week 144	SAFE_L8
53	Listing of COVID-19 Assessments and Symptom Assessments for Subjects with COVID-19 Adverse Events		Week 48 Week 96 Week 144	PAN12

14.12.1.4. Virology

14.12.1.4.1. Tables

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
4.1	Summary of Subject Accountability: Genotypes Available at or prior to Week X	Confirmed Virologic Withdrawal Population	Week 48 Week 96 Week 144	VIRAL_T1
4.2	Summary of Subject Accountability: Phenotypes Available at or prior to Week X	Confirmed Virologic Withdrawal Population	Week 48 Week 96 Week 144	VIRAL_T2
4.3	Summary of IN Mutations at Time of CVW for Subjects Meeting Confirmed Virologic Withdrawal Criteria at or prior to Week X	Confirmed Virologic Withdrawal Population	IDMC Week 48 Week 96 Week 144	VIRAL_T3
4.4	Summary of Treatment-Emergent IN Mutations for Subjects Meeting Confirmed Virologic Withdrawal Criteria at or prior to Week X	Confirmed Virologic Withdrawal Population	IDMC Week 48 Week 96 Week 144	VIRAL_T4
4.5	Summary of Genotypic Data of NRTI, NNRTI, and PI Classes for Subjects Meeting Confirmed Virologic	Confirmed Virologic Withdrawal Population	IDMC Week 48 Week 96 Week 144	VIRAL_T6

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
	Withdrawal Criteria at or prior to Week X			
4.6	Summary of Changes in Major Mutations of NRTI, NNRTI and PI Classes from Baseline at Time of CVW for Subjects with CVW at or prior to Week X	Confirmed Virologic Withdrawal Population	Week 48 Week 96 Week 144	VIRAL_T7
4.7	Summary of Phenotype at Time of CVW for Subjects Meeting Confirmed Virologic Withdrawal Criteria at or prior to Week X by Phenotypic Cut-off	Confirmed Virologic Withdrawal Population	IDMC Week 48 Week 96 Week 144	VIRAL_T8
4.8	Number of Drugs to Which Subjects are Phenotypically Resistant at Time of CVW at or prior to Week X	Confirmed Virologic Withdrawal Population	Week 48 Week 96 Week 144	VIRAL_T9
4.9	Summary of Fold Change to DTG and 3TC at Time of CVW at or prior to Week X	Confirmed Virologic Withdrawal Population	Week 48 Week 96 Week 144	VIRAL_T10

14.12.1.4.2. Other Listings

Number	Title	Details/Comments	Reports	IDSL/TST ID/ Example Shell
54	Listing of All Genotypic Data	ITT-E	Week 48 Week 96 Week 144	VIRAL_L1
55	Listing of Genotypic Data – Confirmed Virological Withdrawal Subjects	Confirmed Virologic Withdrawal Population	IDMC	VIRAL_L2
56	Listing of Genotypic Data and Treatment Emergent Genotypic Mutations – Confirmed Virological Withdrawal Subjects	Confirmed Virologic Withdrawal Population	Week 48 Week 96 Week 144	VIRAL_L3
57	Listing of All Phenotypic Data	ITT-E	Week 48 Week 96 Week 144	VIRAL_L4

Number	Title	Details/Comments	Reports	IDSL/TST ID/ Example Shell
58	Listing of Phenotypic Data for Confirmed Virological Withdrawal Subjects	Confirmed Virologic Withdrawal Population	IDMC Week 48 Week 96 Week 144	VIRAL_L5
59	Listing of Replication Capacity	Confirmed Virologic Withdrawal Population	Week 48 Week 96 Week 144	VIRAL_L6
60	Listing of Genotypic and Phenotypic Data for Subjects with on-treatment Virology Results at non-CVW timepoints	ITT-E	Week 48 Week 96 Week 144	VIRAL_L7

14.12.1.5. Pharmacokinetic

The PK Population will be used, except where noted.

14.12.1.5.1. Tables

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
5.1	Summary of DTG Plasma Concentration-Time Data	Intensive PK population	Week 48	Shell
5.2	Summary of 3TC Plasma Concentration-Time Data	Intensive PK population	Week 48	Shell
5.3	Summary of DTG Concentrations by Visit	Sparse + Trough PK population	Week 48	Shell
5.4	Summary of 3TC Concentrations by Visit	Sparse + Trough PK population	Week 48	Shell
5.5	Summary of Derived DTG Plasma Pharmacokinetic Parameters (non-transformed and log-transformed)	Intensive PK population	Week 48	Shell
5.6	Summary of Derived 3TC Plasma Pharmacokinetic Parameters (non-transformed and log-transformed)	Intensive PK population	Week 48	Shell

14.12.1.5.2. Figures

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
5.1	Individual DTG Plasma Concentration–Time Plot – Intensive Sampling	Intensive PK population	Week 48	Shell
5.2	Individual 3TC Plasma Concentration–Time Plot – Intensive Sampling	Intensive PK population	Week 48	Shell
5.3	Mean DTG Plasma Concentration–Time Plot	Intensive PK population	Week 48	Shell
5.4	Mean 3TC Plasma Concentration–Time Plot	Intensive PK population	Week 48	Shell
5.5	Median DTG Plasma Concentration–Time Plot	Intensive PK population	Week 48	Shell
5.6	Median 3TC Plasma Concentration–Time Plot	Intensive PK population	Week 48	Shell
5.7	Scatter Plot of Individual DTG Concentrations versus Actual Time – Sparse Sampling	Sparse + Trough PK population	Week 48	Shell
5.8	Scatter Plot of Individual 3TC Concentrations versus Actual Time – Sparse Sampling	Sparse + Trough PK population	Week 48	Shell

14.12.1.5.3. Other Listings

Number	Title	Details/ Comments	Reports	IDSL/TST ID/ Example Shell
61	Listing of DTG Plasma Concentration-Time Data	Intensive PK population	Week 48	Shell
62	Listing of 3TC Plasma Concentration-Time Data	Intensive PK population	Week 48	Shell
63	Listing of DTG Plasma Concentrations by Visit	Sparse PK population	Week 48	Shell
64	Listing of 3TC Plasma Concentrations by Visit	Sparse PK population	Week 48	Shell
65	Listing of Derived DTG Plasma Pharmacokinetic Parameters	Intensive PK population	Week 48	Shell
66	Listing of Derived 3TC Plasma Pharmacokinetic Parameters	Intensive PK population	Week 48	Shell