Reporting and Analysis Plan

Study ID: 117172

Official Title of Study: Reporting and Analysis Plan for ING117172 A Phase IIIb, randomized, open-label study of the safety and efficacy of dolutegravir/abacavir/lamivudine once daily compared to atazanavir and ritonavir plus tenofovir/emtricitabine once daily in HIV-1 infected antiretroviral therapy naïve women

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Title	:	Reporting and Analysis Plan for ING117172 A Phase IIIb, randomized, open-label study of the safety and efficacy of dolutegravir/abacavir/lamivudine once daily compared to atazanavir and ritonavir plus tenofovir/emtricitabine once daily in HIV-1 infected antiretroviral therapy naïve women
Compound Number	:	GSK1349572+GR109714+GI265235 (GSK2619619)
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Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Reports for Protocol ING117172.
- This RAP is intended to describe all the planned analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverables.
- The purpose of RAP Amendment 01 (to the originally approved RAP dated 20-OCT-2015) is to provide details on the Final (End of Study) analysis.

Author's Name and Functional Area:

Author	Date
Lead	01-Aug-2022
PPD Associate Statistician, Biostatistics	

RAP Team Reviews:

RAP Team Review Confirmations (Vault TMF):

Reviewer	Date
PPD Principal Programmer/ Analyst, Biostatistics, GSK	19-Aug-2022
PPD Clinical Science Lead, ViiV	19-Aug-2022
PPD Safety Lead, GSK	19-Aug-2022
PPD Clinical Development Leader, ViiV	19-Aug-2022
PPD Clinical Development Manager, ViiV	19-Aug-2022
PPD Study Delivery Lead, GSK	19-Aug-2022

Approval (Vault TMF):

Approver
PPD Manager, Statistics

The main changes included in RAP Amendment 01 are:

Addition of Appendix 13 (Section 12.13) to provide additional details of the planned analyses and data displays for ING117172 Final/End of Study (EoS) reporting.

Appendix 14 (List of data displays) updated to reflect the updates to the EoS analyses in Appendix 13.

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1. CHRONOLOGY

Main RAP	21-OCT-2015	SF_1 00 Reporting and Analysis Plan (RAP)_ARIA_21Oct2015_v1 (Week 48 Interim Analysis)
Amendment 1	DD-MMM-YYYY	Appendix 13 added to provide details of the Analysis Plan for the Final (End of Study) Analysis.

2. REPORTING & ANALYSIS PLAN SYNPOSIS

Overview	Key Elements of the RAP
Purpose	• This RAP describes all the planned analyses and outputs required for the Clinical Study Report(s) for Protocol ING117172.
Protocol	• This RAP is based on protocol amendment 03 [Dated: 19/JUN/2018 of study ING117172 (GSK Document No.:2013N161649_01) and eCRF Version 9.0.
Primary Objective	• To demonstrate the non-inferior antiviral activity of DTG/ABC/3TC FDC once daily compared to ATV+RTV+TDF/FTC FDC each administered once daily over 48 weeks in HIV-1 infected ART naïve women.
Primary Endpoint	• The proportion of subjects with plasma HIV-1 RNA <50 copies/mL at Week 48 using the Snapshot algorithm (Missing, Switch or Discontinuation = Failure) for the ITT-E population.
Study Design	• A 48 week Phase IIIb randomized, open-label, active-controlled, multicenter, parallel group, non-inferiority study. • The study will be conducted in approximately 474 HIV-1 infected ART-naïve women. • Subjects will be randomized 1:1 to receive a FDC of DTG 50mg/ ABC 600mg/ 3TC 300mg once daily or ATV 300mg plus RTV 100mg and TDF 300mg/ FTC 200mg FDC each administered once daily. • Randomization will be stratified by Screening plasma HIV-1 RNA (≤100,000 copies/mL [c/mL] or >100,000 c/mL) and CD4+ cell count (≤350 cells/mm3 or >350 cells/mm3). • The study will comprise a Screening Phase (approximately 14-28 days), a Randomized Phase (48 weeks), and a Continuation Phase. • No dose reductions, modifications in dosage, or changes in the frequency of dosing of any components of each regimen will be allowed in this study.
Planned Analyses	• The main analysis will be conducted to evaluate the primary objective of the protocol when all subjects have completed their Week 48 visit. A final analysis will be conducted when all subjects have completed the study. Further data cuts and analyses may be conducted as necessary in order to support regulatory submissions and publications and pricing reimbursement dossiers.
Analysis Populations	• The Intent-to-Treat Exposed (ITT-E) Population will be used for summaries of efficacy and study population. The Safety Population will be used for

Overview	Key Elements of the RAP
	summaries of safety. • A 'Per-Protocol' Population and an Intent-to-Treat Population will be used to evaluate efficacy in sensitivity analyses. • Separate populations for virology analyses will also be defined.
Hypothesis	• This study is designed to show that the antiviral effect of the DTG/ABC/3TC FDC administered once daily is non-inferior to once daily ATV+RTV+TDF/FTC FDC. Non-inferiority can be concluded if the lower bound of a two-sided 95% confidence interval for the difference in response rates between the two treatment arms is greater than -12%.
Primary Analyses	• The primary endpoint will be analyzed using a Cochran-Mantel-Haenszel stratified analysis, adjusting from baseline stratification factors. A point estimate and corresponding 95% confidence interval will be constructed for the adjusted difference in response rates between DTG and ATV treatment groups. • The primary analysis will be based on the ITT-E population using the Snapshot dataset. The primary comparison will be made at a one-sided 2.5% level of significance.
Secondary Analyses	• Proportion of subjects with plasma HIV-1 RNA <50 and <400 c/mL over time • Absolute values and changes from baseline in plasma HIV-1 RNA over time • Absolute values and changes from baseline in CD4+ cell counts over time • Incidence of HIV-1 disease progression • Safety data will be presented in tabular format and summarized descriptively according to GSK's Integrated Data Standards Library (IDSL) standards. • Change from baseline in fasting lipids.

3. SUMMARY OF KEY PROTOCOL INFORMATION

3.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in protocol amendment 1 (Dated: 12/AUG/2013).

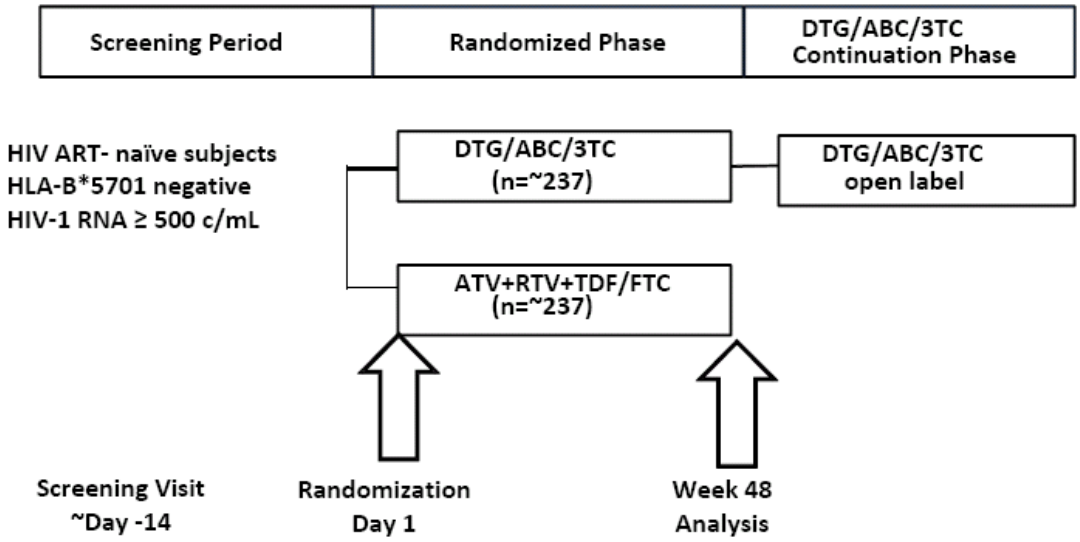
3.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To demonstrate the non-inferior antiviral activity of DTG/ABC/3TC FDC once daily compared to ATV+RTV+TDF/FTC FDC each administered once daily over 48 weeks in HIV-1 infected ART naïve women.	• The primary endpoint for this study will be the proportion of subjects with plasma HIV-1 RNA <50 copies/mL at Week 48 using the Snapshot algorithm (Missing, Switch or Discontinuation = Failure) for the ITT-E population
Secondary Objectives	**Secondary Endpoints**
• To evaluate the antiviral and immunological activity and incidence of disease progression (HIV-associated conditions, AIDS and death) of DTG/ABC/3TC FDC once daily compared to ATV+RTV+TDF/FTC FDC once daily over time;	• Proportion of subjects with plasma HIV-1 RNA <50 and <400 c/mL over time; • Absolute values and change from Baseline in plasma HIV-1 RNA over time; • Absolute values and changes from Baseline in CD4+ cell counts over time; • Incidence of disease progression (HIV-associated conditions, AIDS and death).
• To compare the safety, tolerability, and laboratory parameters of DTG/ABC/3TC FDC once daily to ATV+RTV+TDF/FTC FDC once daily over time;	• Incidence and severity of AEs and laboratory abnormalities; • Absolute values and changes over time in laboratory parameters; • Proportion of subjects who discontinue treatment due to AEs; • Change from Baseline in fasting lipids and glucose;
• To assess the development of viral resistance in subjects who meet confirmed virologic withdrawal criteria;	• Incidence of treatment-emergent genotypic and phenotypic resistance in subjects who meet confirmed virologic withdrawal criteria.
• To evaluate renal markers (in urine and blood), and bone markers (in blood) in subjects treated with DTG/ABC/3TC FDC compared to ATV+RTV+TDF/FTC FDC;	• Changes from Baseline in renal and bone markers.
• To assess treatment satisfaction, and change in health-related quality-of-life for subjects treated with DTG/ABC/3TC FDC compared to ATV+RTV+TDF/FTC FDC;	• Change from Baseline in health related quality of life using SF-12 at Week 48. • Treatment satisfaction for subjects treated with DTG/ABC/3TC FDC once daily and those treated with ATV+RTV+TDF/FTC FDC once daily at weeks 4, 12, 24, and 48 (or withdrawal from the study).

Objectives	Endpoints
• To evaluate the effect of patient characteristics (i.e., demographic factors, HIV-1 subtype, Baseline CD4) on response to DTG/ABC/3TC FDC compared to ATV+RTV+TDF/FTC FDC over time.	• Proportion of subjects with plasma HIV-1 RNA <50 c/mL over time by subgroups.

3.3. Study Design

Overview of Study Design and Key Features



Design Features	• 48 week Phase IIIb randomized, open-label, active-controlled, multicenter, parallel group, non-inferiority study. The study comprises a Screening Phase (approximately 14-28 days), a Randomized Phase (48 weeks), and a Continuation Phase.
Dosing	• Randomized Phase: DTG/ABC/3TC FDC 50mg/600mg/300mg once daily or ATV (300mg) +RTV (100mg) +TDF/FTC FDC (300mg/200mg) all administered once daily, up to Week 48. • Continuation Phase: Only subjects randomized to the DTG/ABD/3TC FDC arm can continue past Week 48 in an open-label continuation phase.
Treatment Assignment	• N=474 randomized 1:1 across two treatment arms. • Randomization stratified by Screening plasma HIV-1 RNA (≤100,000 copies/mL [c/mL] or >100,000 c/mL) and CD4+ cell count (≤350 cells/mm3 or >350 cells/mm3). • GSK RandAll NG used to generate randomisation schedules. • Centralised randomization using GSK RAMOS for treatment allocation.
Interim Analysis	• The main analysis will be conducted to evaluate the primary objective of the protocol when all subjects have completed their Week 48 visit. Further data cuts and analyses may be conducted as necessary in order to support regulatory submissions and publications.

3.4. Statistical Hypotheses

This study is designed to show that the antiviral effect of the DTG/ABC/3TC FDC administered once daily is non-inferior to once daily ATV+RTV+TDF/FTC FDC.

Non-inferiority can be concluded if the lower bound of a two-sided 95% confidence interval for the difference in response rates between the two treatment arms is greater than -12%. If r_d is the response rate on DTG/ABC/3TC FDC and r_a is the response rate on ATV+RTV+TDF/FTC FDC then the hypotheses can be written as follows:

$$H0: r_d - r_a \leq -12\% \qquad H1: r_d - r_a > -12\%.$$

4. PLANNED ANALYSES

4.1. Interim Analyses

The main analysis will be conducted to evaluate the primary objective of the protocol when all subjects have completed their Week 48 visit. Further data cuts and analyses may be conducted as necessary in order to support regulatory submissions and publications.

The planned primary analyses will be performed after the completion of the following sequential steps:

1. All subjects have completed the Week 48 visit as defined in the protocol.
2. All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.
3. All criteria for unblinding the randomisation codes have been met.
4. Randomisation codes have been distributed according to RandAll NG procedures.

4.2. Final Analyses

A final End-of-Study analysis will be conducted when all subjects have completed the study.

Details of which outputs will be produced at Week 48 and End of Study can be found in Section 12.14.

5. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Subjects Screened	• Comprised of all subjects screened for inclusion in the study. • Subjects may be re-screened once, for which they will receive a new subject number. • Only the latest re-screening data will be included in the screening population summaries/analyses but all screening data will be listed.	• Study Population
Safety	• Comprise of all subjects who receive at least one dose of study treatment. • This population will be based on the treatment the subject actually received. If a subject receives treatment differing from that assigned by the randomization schedule (for either a portion of or the entire time on study), they will be analysed based on the treatment taken for the majority of study participation.	• Safety
Intent-To-Treat (Exposed)	• Comprise of all randomized subjects who receive at least one dose of study treatment. • This population will be based on the treatment to which the subject was randomized. • Any subject who receives a treatment randomization number will be considered to have been randomized.	• Efficacy • Study Population • Health Outcomes
Intent-To-Treat	• Comprise of all randomized subjects. • This population will be based on the treatment to which the subject was randomized. • Any subject who receives a treatment randomization number will be considered to have been randomized.	• Efficacy (sensitivity analyses)
Per-Protocol	• Comprise of all subjects in the ITT-E population with the exception of major protocol violators, e.g. violations which could affect the assessment of antiviral activity. • Protocol deviations that would exclude subjects from the PP population are defined in Section 5.1(Protocol Deviations) and Appendix 1 (Protocol Deviation Management and Definition for Per-Protocol Population).	• Efficacy (sensitivity analyses)

Population	Definition / Criteria	Analyses Evaluated
Viral Genotypic	• Comprise of all subjects in the ITT-E population with available On-treatment genotypic resistance data at the time confirmed virologic withdrawal criterion is met (see protocol, Section 4.5.1).	• Genotypic
Viral Phenotypic	• Comprise of all subjects in the ITT-E population with available On-treatment phenotypic resistance data at the time confirmed virologic withdrawal criterion is met (see protocol, Section 4.5.1).	• Phenotypic

1. **NOTES :**

- Please refer to Appendix 14: List of Data Displays which details the population to be used for each displays being generated.

5.1. Protocol Deviations

- 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 will also be summarised and listed. (Please refer to Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population)].
- Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan.
    - Data will be reviewed prior to unblinding and freezing the database to ensure all important deviations and deviations which may lead to exclusion from the analysis are captured and categorised on the protocol deviations dataset.
    - This dataset will be the basis for the summaries and listings of protocol deviations.
- A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

6. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

- There are no planned adjustments made for multiple centres in this study.
- There are no planned adjustments for multiple comparisons or multiplicity.
- There are no PK analyses planned in this study.

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
12.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
12.2	Appendix 2: Time & Events
12.3	Appendix 3: Assessment Windows
12.4	Appendix 4: Treatment States and Phases
12.5	Appendix 5: Data Display Standards & Handling Conventions
12.6	Appendix 6: Derived and Transformed Data
12.7	Appendix 7: Premature Withdrawals & Handling of Missing Data
12.8	Appendix 8: Values of Potential Clinical Importance
12.9	Appendix 9: Examination of Covariates and Subgroups
12.10	Appendix 10: Model Checking and Diagnostics for Statistical Analyses
12.11	Appendix 11: Snapshot
12.12	Appendix 12: Abbreviations & Trade Marks
12.13	Appendix 13: Final (End of Study) Analysis
12.14	Appendix 14: List of Data Displays
12.15	Appendix 15: Example Mock Shells for Data Displays

7. STUDY POPULATION ANALYSES

7.1. Overview of Planned Analyses

The study population analyses will be based on the ITT-E population, and will include a total column, unless otherwise specified. All displays are for the randomised phase only, unless otherwise stated.

Table 2 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses

Display Type	Data Display's Generated	
	Table	Listing
Randomisation		
Randomisation		Y [1]
Subject Disposition		
Study Populations [2]	Y	Y [3]
Study Recruitment [2]		Y
Age Categories	Y	
History of Rescreened Subjects		Y
Reasons for Screen Failure [2]	Y	Y
Subject Disposition	Y [4,9]	
Reasons for Withdrawal by Visit	Y	Y
Study Visit Dates		Y
Important Protocol Deviations	Y	Y
Deviations leading to exclusion from PP	Y	Y
Inclusion and Exclusion Criteria Deviations		Y
Demography		
Demographic Characteristics[10]	Y	Y
Race & Racial Combinations[11]	Y	Y
Hepatitis Status	Y	Y
CDC Classification of HIV infection	Y	Y
HIV Risk Factor	Y	Y
Cardiovascular Risk Assessments at Day 1	Y	Y
Distribution of Quantitative Plasma HIV-1 RNA	Y	
Distribution of CD4+ Cell Counts	Y	
History of Cardiac Therapeutic Procedures		Y

Display Type	Data Display's Generated	
	Table	Listing
Medical Conditions, Concomitant Medications & Antiretroviral Therapy		
Medical Conditions (Current and Past) [12]	Y	Y[8]
Medical Conditions: Sub-conditions (Current/Past) [12]	Y	Y[8]
Concomitant Medications (non-ART)	Y[5]	Y[6,8]
Prior and Concomitant ART Medications		Y[7,8]
Lipid Modifying agents (Baseline and Post-Baseline)	Y	
Other		
IP Accountability [13]		Y

1. NOTES :

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

1. One listing of subjects randomised but not treated, and one listing of planned and actual treatment strata.
2. All Subjects screened population.
3. Listing only includes those who were excluded from at least one population.
4. Randomised Phase only at Week 48 analysis; Combined Randomised Phase and Continuation Phase for End of Study analysis.
5. 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).)
6. One listing for concomitant non-ART medications and one listing showing the relationship between verbatim text, ingredient and ATC Level 1.
7. One listing for Prior ART, one listing for concomitant ART and one listing showing the relationship between verbatim text, ingredient, combination and ATC Level 4.
8. Repeated for subjects at Mexico sites who experienced an adverse event, at End of Study reporting only.
9. Subjects who have not been recorded as either completing or withdrawing from the study will be categorized as "Ongoing at time of the analysis" for summary purposes.
10. Age, ethnicity, weight and height collected at screening (Day 1 for height)
11. 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.
12. Medical conditions will be coded using the Medical Dictionary for Regulatory Activities (MedDRA).
13. Dispensation information (dates and number of tablets dispensed and returned)

8. PRIMARY STATISTICAL ANALYSES

8.1. Efficacy Analyses

The primary efficacy analyses will be based on the Intent-To-Treat (Exposed) population, unless otherwise specified. Summaries will be presented by treatment group with no total column.

All displays are for the randomised phase only, unless otherwise stated.

8.1.1. 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: List of Data Displays.

Table 3 Overview of Planned Efficacy Analyses

Endpoints	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Proportion of Subjects with Plasma HIV-1 RNA <50c/ml at Week 48 – Snapshot							
Primary Analysis	Y[1]			Y[2]	Y[3]		Y[2]
Treatment Heterogeneity across randomization strata	Y						
<50 c/mL by Subgroups [4]				Y	Y[5]		
Proportion of subjects without virologic (ERDF) or virologic/tolerability (TRDF) failure – Sensitivity analysis							
Kaplan-Meier estimates				Y			

1. NOTES :

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

1. Generated using the 'Intent-to-Treat Exposed' (primary), 'Per-Protocol' and 'Intent-to-Treat' (sensitivity) populations.
2. Study outcomes (i.e., response below 50 c/mL, virologic failure or reason for no data in the window) based on the snapshot algorithm.
3. Line plots, with 95% confidence intervals, for the proportion of subjects below 50 c/mL by treatment group at each visit.
4. Baseline demography (age, race, country, CDC), HIV-1 subtype, Baseline CD4 and Baseline viral load
5. Plot of 95% confidence intervals for the proportion of subjects below 50 c/mL by subgroup.

8.1.2. Planned Efficacy Statistical Analyses

Primary Statistical Analyses

Endpoint

- Proportion of subjects with plasma HIV-1 RNA <50 c/mL at Week 48 using the Snapshot algorithm (Missing, Switch or Discontinuation = Failure) 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 success or failure 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 Section 12.3.1)
- Full details of the Snapshot algorithm are in Appendix 11.

Model Specification

- The primary endpoint will be analysed using a stratified analysis with Cochran-Mantel-Haenszel (CMH) weights, adjusting for Baseline plasma HIV-1 RNA ($\leq$ vs. >100,000 c/mL) and CD4+ cell count ($\leq$350 cells/mm3 or >350 cells/mm3).
- The CMH estimate of the adjusted treatment difference will be calculated as a weighted average of strata-specific estimates of the treatment difference calculated within each of the following four Baseline analysis strata:
    - Plasma HIV-1 RNA $\leq$ 100,000 c/mL AND CD4+ $\leq$ 350 cells/mm3
    - Plasma HIV-1 RNA $\leq$ 100,000 c/mL AND CD4+ > 350 cells/mm3
    - Plasma HIV-1 RNA > 100,000 c/mL AND CD4+ $\leq$ 350 cells/mm3
    - Plasma HIV-1 RNA > 100,000 c/mL AND CD4+ > 350 cells/mm3
- If n_k is the number of DTG treated subjects, m_k is the number of ATV treated subjects, and $N_k = n_k + m_k$ is the total number of subjects in the *k*th stratum, then the CMH estimate is given by

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

where,

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

are CMH weights and d_k are estimates of the differences in response proportions between the

Primary Statistical Analyses

two treatment arms, r_d-r_a, for the *k*th strata.

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

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

using the variance estimator, var(d_{cmh}), given by [Sato, 1989], which is consistent in both sparse data and large strata. The full equation for this variance estimate is provided in Section 12.6.4.

Model Results Presentation

- Adjusted CMH estimate of the difference in the proportion of responders between each treatment group (DTG – ATV) and corresponding 95% confidence interval.
- Non-inferiority will be concluded if the lower bound of the two-sided 95% confidence interval (CI) for the CMH adjusted difference in the proportion of patients who respond in the DTG group minus the proportion of patients who respond in the ATV group is greater than -12%.

Sensitivity and Supportive Statistical Analyses

1. Treatment Heterogeneity across randomization strata:
   - The weighted least squares chi-squared statistic [Fleiss, 1981] will be used to test for one-way homogeneity across the levels of each categorical variable, with each categorical variable considered separately.
   - Following Lui and Kelly [Lui, 2000] ½ will be added to each cell in any strata for which the stratum-specific rate estimates of either rd or ra are zero or one, and tests will be one-sided.
   - Any heterogeneity found to be statistically significant will be explored and if necessary results will be reported for each level of the categorical variable. Investigation of heterogeneity will be confined to the primary. Tests of homogeneity will be assessed at the one-sided 10% level of significance.

2. Per-protocol population analysis:
   - To assess the impact of major protocol deviations, statistical analysis will be repeated using the Per-protocol population and compared for consistency with the results from the primary ITT-E population analysis. If both analyses show non-inferiority then the hypothesis that the antiviral effect of treatment with DTG/ABC/3TC FDC is superior to treatment with ATV+RTV+TDF/FTC FDC will be tested at the two-sided 5% level of significance. Superiority will be declared if the lower end of the confidence interval is above 0% for the ITT-E population analysis. If superiority is declared the p-value for superiority will also be calculated.

3. Intent-to-Treat population analysis:
   - Statistical analysis will be repeated using the Intent-to-Treat population and compared for consistency with the results from the ITT-E and PP populations.
   - In this analysis, subjects randomised but not exposed to study treatment will be classified as non-responders, which therefore address any selection bias that may occur given the open-label study design.

Sensitivity and Supportive Statistical Analyses

4. Exploration of Subgroups:
   - A simple analysis for all the subgroups listed in Section 12.9.1 will be performed. This will show the proportion of subjects with plasma HIV-1 RNA <50 c/mL at the time of analysis (Week 48) based on the SNAPSHOT algorithm and will be presented by treatment group.
   - Unadjusted difference in proportions between treatment groups and corresponding two-sided 95% CI will also be presented by treatment and subgroup, and a 95% CI for the (unadjusted) treatment difference in each subgroup. These results will also be presented graphically.
   - If the basic summary suggests an interaction, then a corresponding summary of study outcomes (i.e., response below 50 c/mL, virologic failure or reason for no data in the window) by subgroup will be produced.

   Note: These subgroup analyses will be exploratory and likely underpowered so that interpretation may therefore focus on point estimates as well as the lower bounds of 95% CIs for the treatment differences and response rates. Additionally, multiple comparisons are being made which inflates the risk of false positive findings. Therefore, if consistent findings across the multiple comparisons were observed then these analyses would still be suggestive of a generalizable finding of non-inferiority.

5. Proportion of subjects without virologic (ERDF) or virologic/tolerability (TRDF) failure:
   - Estimated using the Kaplan-Meier nonparametric method based on the time to Confirmed Virologic Withdrawal (CVW) or treatment related/efficacy related discontinuation (i.e., drug-related AE, protocol defined safety stopping criteria, or lack of efficacy)
   - Subjects who have not met CVW criteria and are ongoing in the study, or who have discontinued for reasons other than those related to treatment/lack of efficacy, will be censored.
   - The estimate of the standard error used to derive confidence intervals for the difference in proportions between treatment groups will be based on Greenwood's formula [Kalbfleisch, 1980]
   - The estimated proportion of subjects without Confirmed Virologic Withdrawal and not discontinued due to treatment related/efficacy related reasons at Week 48 will be presented by treatment group, along with estimated difference in proportions between treatment groups and its associated two-sided 95% CI.
   - The proportion of subjects with Confirmed Virologic Withdrawal will be summarized by visit.

9. SECONDARY STATISTICAL ANALYSES

9.1. Efficacy Analyses

9.1.1. Overview of Planned Efficacy Analyses

The secondary efficacy analyses will be based on the Intent-To-Treat (Exposed) population, unless otherwise specified. All displays are for the randomised phase only, unless otherwise stated.

Table 4 provides an overview of the planned efficacy analyses, with further details of data displays being presented in Appendix 14: List of Data Displays.

Table 4 Overview of Planned Efficacy Analyses

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Plasma HIV-1 RNA Over Time														
Observed				Y		Y[1]	Y				Y			
Proportion of Subjects with Plasma HIV-1 RNA <400 & <50 copies/mL - Snapshot														
<50 c/mL by Visit				Y[2]										
<400 c/mL by Visit				Y										
<400 c/mL Outcomes				Y			Y							
Confirmed Virologic Withdrawal (CVW)														
CVW by Visit				Y			Y							
HIV-1 RNA distribution at time of suspected and confirmed Virologic withdrawal				Y										
CD4+ Cell Counts Over Time														
CD4+ Observed				Y			Y				Y			Y
Post-baseline HIV-1 Disease Progression[3]														
HIV Conditions including Recurrences				Y			Y							
HIV Conditions excluding Recurrences				Y										
HIV Disease Progressions				Y										

NOTES :

- T = Table, F = Figures, L = Listings, Y = Yes display generated
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- Individual = Represents FL related to any displays of individual subject observed raw data.

1. Individual plasma profiles
2. Repeated for End of Study using Observed data.
3. HIV disease progressions categories: CDC Category A at baseline to CDC Category B event; CDC Category A at baseline to CDC Category C event; CDC Category B at baseline to CDC Category C event; CDC Category C at baseline to new CDC Category C event and CDC Category A, B or C at baseline to death.

9.2. Safety Analyses

9.2.1. Overview of Planned Analyses

The safety analyses will be based on the Safety population, presented by treatment group with a total column unless otherwise specified.

The observed case (OC) dataset will be used, which contains the data that is available at a particular timepoint, with no imputation for missing values, unless otherwise stated.

All displays are for the randomised phase only, unless otherwise stated.

Table 5 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 14: List of Data Displays.

Table 5 Overview of Planned Safety Analyses

Endpoint	Absolute				Change from Baseline				Max Post BL			
	Summary		Individual		Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L	T	F	F	L
Exposure												
Extent of Exposure	Y[1]			Y[2,14]								
Adverse Events[3]												
All AEs by SOC and Toxicity[5]	Y			Y[4]								
Common AEs by freq [6]	Y	Y[16]										
Common Grade 2-4 AEs [6]	Y											
All Drug-Related AEs by SOC and toxicity[5]	Y											
Common Drug-related Grade 2-4 AEs [6]	Y											
All SAEs by SOC	Y[1]											
Reason for Considering as a Serious Adverse Event (FDA)				Y								
All Drug-Related SAEs	Y											

Endpoint	Absolute				Change from Baseline				Max Post BL			
	Summary		Individual		Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L	T	F	F	L
by SOC												
Fatal SAEs				Y								
Non-Fatal SAEs				Y								
Withdrawal AEs	Y[1]			Y								
Common Non-Serious AEs (FDAAA)	Y											
Number of occurrences of Common Non-serious AEs by SOC (EudraCT)	Y											
Number of occurrences of SAEs, Drug-related AEs, Fatal SAEs, and Drug-related SAEs (EudraCT)	Y											
AEs of Subjects at Mexico sites				Y[18]								
SAEs of Subjects at non-Mexico sites				Y[18]								
Pre-treatment AEs				Y								
CV events				Y								
PSRAE				Y[17]								
Laboratory Values Over Time												
Clinical Chemistry				Y [7]	Y							
Lipids (%)					Y							
Fasted Lipid (Triglycerides and TC/HDL ratio) analysis					Y[22]							
Hematology				Y [7]	Y							
Urine Dipstick				Y [7]	Y					Y		
Urine Concentration				Y [7]	Y							
Proteinuria shifts										Y[9]		
Liver Chemistries										Y[8]		
NCEP shifts in lipids									Y	Y[10]		
Total Cholesterol/HDL ratio					Y							
Bone markers					Y							

Endpoint	Absolute				Change from Baseline				Max Post BL			
	Summary		Individual		Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L	T	F	F	L
Treatment Emergent Laboratory Toxicities[11]												
Clinical Chemistry									Y			
Hematology									Y			
Other												
ECG Findings				Y[21]								
Vital Signs				Y								
Abacavir HSR	Y			Y [12]								
Liver Assessment				Y [13]								
Hepatobiliary Abnormality criteria	Y [1,19]											
Columbia suicidality	Y			Y [15]								
Subjects who became Pregnant				Y								
Patient Profiles				Y [20]								

NOTES :

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

1. Randomisation Phase only at Week 48 analysis; Combined Randomisation Phase and Continuation Phase for End of Study analysis.
2. Includes reason for any dose change/interruption.
3. Adverse events will be coded using the MedDRA coding dictionary to give a preferred term and a system organ class. Summaries include only Post-baseline AEs with onset date up to cut-off date for reporting effort, listings include all AEs including those with onset pre- or post-treatment.
4. One listing of all AEs including verbatim text and preferred term, one showing the relationship between verbatim text, preferred term and SOC and another giving subject numbers for individual all treatment emergent AEs.
5. For AEs reported more than once by a subject, the most severe intensity will be included.
6. Common AEs are those with >5% incidence in either treatment group summarised by frequency.
7. Listings for subjects with abnormalities for potential clinical concern, defined as any Grade1-4 toxicity.
8. Scatter plot of baseline vs. maximum post-baseline for ALT. Scatter plot of maximum ALT vs. maximum Bilirubin.
9. Shift table summarising baseline vs. maximum post-baseline result for urine dipstick protein
10. Bar chart for LDL, HDL, TC, Trig and HDL/TC ratio.
11. Treatment Emergent Laboratory Toxicities - See protocol Section 11.2, Appendix 2.
12. Separate listings for exposure to abacavir, history of drug allergies, family conditions, skin rash, symptoms, vital signs, individual symptoms and diagnostic category assignment.
13. Separate listings for time of event from trt, RUCAM score, biopsy, imaging, past/ current conditions & FU
14. Repeated for subjects at Mexico sites at End of Study reporting.
15. Includes Baseline and lists all visits for a subject who reports any ideation or behaviour at any visit.
16. Plots of incidence rates and relative risk with 95% CI for DTG vs. ATV.
17. Four PSRAE listings: Event and Description (Section 1- Section 2), Possible Cause (Section 3), Section 4 and Section 5- Section 8.
18. Only for End of Study reporting
19. One summary of subjects and another table showing Subject Ids.
20. Patient profiles for subjects meeting protocol defined liver stopping criteria and for patients with virologic failure. Patient profiles can also be provided for any other subjects, as necessary for medical review.

21. Only collected when a Cardivascular event occurs.
22. Primary analysis method is multiple imputation MAR. Repeated for sensitivity analyses using OC, LOCF and MMRM.

9.2.2. Planned Safety Statistical Analyses

Statistical Analyses
Endpoints
• Change from Baseline in fasted triglycerides at Week 48. • Change from Baseline in fasted TC/HDL ratio at Week 48.
Covariates
• Baseline Plasma HIV-1 RNA (≤100,000 c/mL c/mL or >100,000 c/mL c/mL) • Baseline CD4+ cell count (≤350 cells/mm3 cells/mm3 or >350 cells/mm3) • Fasted triglycerides (mmol/L) and fasted TC/HDL measurements at Baseline, Week 12 and Week 36 • Age (>=50 or <50)
Data Handling
• If a subject is on lipid-lowering therapy from Baseline, they will be excluded from the analysis. • If a subject initiates lipid-lowering therapy during the study, all visits after that date will be set to missing. • All other data remains as is (observed or missing). • A multiple imputation technique will be used to deal with the missing data at week 48.
Model Specification
• Multiple imputations will be drawn from a multivariate normal model for the data (including covariates) with a Markov Chain Monte Carlo (MCMC) approach used to estimate posterior distributions. A non informative prior will be used. A seed of 18 will be used in the SAS program. Where a subject has a monotone or non-monotone pattern of missingness, all of their missing observations can be imputed under this approach. • Imputations will be drawn separately for subsets of subjects according to their treatment group, i.e., based on means and variance-covariances from the same treatment group (Missing At Random (MAR) approach) conditioning on observed covariates listed above. This will be known as the MAR method. • The imputations will be carried out 1,000 times. An ANOVA will be performed on each datasets produced adjusting for baseline triglycerides (<5.65 mmol/L or ≥5 .65 mmol/L) or TC/HDL ratio (<3.5 or ≥3.5), age, baseline plasma HIV-1 RNA and CD4+ cell count, regardless of their significance. PROC MIANALYZE in SAS will be used to combine the 1,000 estimated means and difference to produce one estimated mean with 95% CI and associated p-value for the adjusted mean difference between each treatment group at Week 48. • Interactions between treatment and each of the covariates will not be assessed.
Model Checking & Diagnostics
• Refer to Appendix 10: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Adjusted means and corresponding standard error of means (SEs) will be presented for each treatment, together with estimated treatment difference (DTG – ATV) and corresponding 95% confidence interval and p-value.

Statistical Analyses
Sensitivity Analyses

• Two ANCOVA sensitivity analyses will be performed as follows:
  ◦ using the standard Observed Case (OC) dataset, with no adjustment or imputation for withdrawing, initiating lipid-lowering agents or other missing data.
  ◦ using the Lipid LOCF dataset (see Section 12.7.2.2), but also carrying forward the last observation to any missing visits.
• A MMRM analysis, with time crossed with treatment, age, baseline triglycerides (<5.65 mmol/L or ≥5 .65 mmol/L) or TC/HDL ratio (<3.5 or ≥3.5),baseline Plasma HIV-1 RNA and CD4+ cell count will also be conducted.

10. OTHER STATISTICAL ANALYSES

10.1. Health Outcomes

The Health Outcomes analyses will be based on the ITT(E) population and presented by treatment group unless otherwise specified.

All displays are for the randomised phase only, unless otherwise stated.

Table 6 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 14: List of Data Displays.

Table 6 Overview of Planned Health Outcome Analyses

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Quality of Life														
SF-12 individual item scores by Visit - LOCF				Y										
SF-12 Total score, PCS and MCS by Visit - LOCF & Observed				Y							Y[1]			
Treatment satisfaction														
HIVTSQs individual item scores by Visit - LOCF				Y			Y							
HIVTSQs (at Weeks 4, 12, 24 and 48) - LOCF & Observed	Y[2]						Y							

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

1. Change from Baseline at Week 48
2. Separate summaries for Total score, Lifestyle/ease sub-score and General Satisfaction/Clinical sub-score.

Statistical Analyses
Endpoint(s)
• HIVTSQ total score • HIVTSQ general satisfaction/clinical sub-score (items 1, 2, 3, 9, and 10) • HIVTSQ lifestyle/ease sub-scores (items 4, 5, 6, 7 and 8)
Model Specification/Analysis Methodology
• Wilcoxon rank sum tests. • No adjustment for multiplicity will be applied as these analyses will be considered exploratory. • An LOCF dataset will be used as described in Section 12.7.2.2. • The analysis will be repeated using an Observed Case dataset (as supportive analyses). No adjustment for

multiplicity will be applied as these analyses will be considered supportive.
Model Results Presentation
• Summary statistics will be presented by treatment group, with a p-value for the difference in the mean based on the Wilcoxon rank sum test.

10.2. Virology

The virology analyses of genotype data will be based on the Genotypic population, and analyses of phenotype data will be based on the Phenotypic population. Summaries will be presented by treatment group unless otherwise specified.

All displays are for the randomised phase only, unless otherwise stated.

Table 7 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 14: List of Data Displays.

Table 7 Overview of Planned Virology Analyses

Endpoint	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Genotypic resistance								
Incidence of genotype at time of CVW[3]	Y[1]			Y	Y[1]			Y
Phenotypic resistance								
Incidence of phenotype at time of CVW[3]	Y[2[			Y				
INI replication capacity at time of CVW[3]				Y				
Fold Change at time of CVW[3]	Y				Y			

1. NOTES :
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- Individual = Represents FL related to any displays of individual subject observed raw data.

1. Separate outputs for INI and NRTI/NNRTI/PI mutations

2. Separate outputs by phenotypic cut-off and by number of drugs to which subjects are resistant.

3. 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.

11. REFERENCES

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12. APPENDICES

Section	Appendix
RAP Section 5 : Analysis Populations	
Section 12.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
RAP Section 6 : General Considerations for Data Analyses & Data Handling Conventions	
Section 12.2	Appendix 2: Time and Events
Section 12.3	Appendix 3: Assessment Windows
Section 12.4	Appendix 4: Treatment States & Phases
Section 12.5	Appendix 5: Data Display Standards & Handling Conventions • Study Treatment & Sub-group Display Descriptors • Baseline Definitions & Derivations • Reporting Process & Standards
Section 12.6	Appendix 6: Derived and Transformed Data • General, Study Population & Safety • Efficacy • Virology • Health outcomes
Section 12.7	Appendix 7: Premature Withdrawals & Handling of Missing Data • Premature Withdrawals • Handling of Missing Data
Section 12.8	Appendix 8: Values of Potential Clinical Importance
Section 12.9	Appendix 9: Examination of Covariates and Subgroups
Section 12.10	Appendix 10: Model Checking and Diagnostics for Statistical Analyses
Section 12.11	Appendix 11: Snapshot
Other RAP Appendices	
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Section 12.13	Appendix 13: Final (End of Study) Analysis
Section 12.14	Appendix 14: List of Data Displays
Section 12.15	Appendix 15: Example Mock Shells for Data Displays

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

12.1.1. Exclusions from Per Protocol Population

Protocol deviations leading to exclusion from PP population are those deviations which

- may directly impact the efficacy endpoint of HIV-1 RNA; or
- lead to permanent discontinuation of IP/withdrawal and hence indirectly impact the efficacy endpoint by causing data to be missing.

The following criteria define the protocol deviations which, if they occur prior to an analysis timepoint of interest, will lead to exclusion of a subject from the Per-Protocol population for that analysis. Potential protocol deviations leading to exclusion from PP population will be reviewed by the study team to confirm that they meet these criteria. This review will occur before the clinical database has been frozen for analysis.

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

Number	Exclusion Description
01	Subject deviates from any inclusion or exclusion criteria, as recorded in the eCRF
02	Subject took/received incorrect IP, i.e., other than the one to which they were randomized for greater than 10% of the total time On-treatment
03	Interruption of IP for greater than 10% of the total time On-treatment, for reasons other than treatment-related adverse events/laboratory abnormalities, based on eCRF IP exposure forms (or CONMEDS eCRF forms for locally prescribed RTV during supply issues)
04	Prohibited medications: Receiving ART medication other than that prescribed/allowed by the study for a duration of >2 consecutive weeks or receiving non-ART medication that would potentially impact exposure or response to therapy with duration taken into consideration
05	Permanent discontinuation of IP/withdrawal due to a reason of “Protocol Deviation” (as recorded in the eCRF).

12.2. Appendix 2: Time & Events

12.2.1. Protocol Defined Time & Events

Procedures	Screen[a]	Day 1	Randomized Phase						Continuation Phase[k]	Withdrawal	Follow-up[l]
			Clinic Visits					Contact at Wk 8 18, 30, 42[r]	Every 12 weeks after Week 48		
			Week 4	Week 12	Week 24	Week 36	Week 48				
Clinical and Other Assessments											
Written informed consent	X										
Inclusion/Exclusion criteria[b]	X	X									
Demography	X										
Prior ART history	X										
Medical history[c]		X									
Current medical conditions		X									
HIV risk factors and mode of transmission		X									
CDC HIV-1 classification	X	X									
HIV associated conditions			X	X	X	X	X		X	X	
Cardiovascular risk assessment[d]		X									
Columbia Suicidality Severity Rating Scale		X[u]	X	X	X	X	X		X	X	
Concomitant medication	X	X	X	X	X	X	X		X	X	X
Limited physical examination[s]	X	X	X	X	X	X	X		X	X	X
12-lead ECG[t]	X										
Adverse events		X	X	X	X	X	X	X	X	X	X
Serious adverse events	X[j]	X	X	X	X	X	X	X	X	X	X
SF-12[w]		X			X		X			X	
HIVTSQ[w]			X	X	X		X			X	
Confirm understanding of study and management/tolerability of regimen		X	X	X	X	X	X	X	X		
Laboratory Assessments											
Plasma for HIV genotyping	X										

Procedures	Screen[a]	Day 1	Randomized Phase						Continuation Phase[k]	Withdrawal	Follow-up[l]
			Clinic Visits					Contact at Wk 8 18, 30, 42[r]	Every 12 weeks after Week 48		
			Week 4	Week 12	Week 24	Week 36	Week 48				
Quantitative plasma HIV-1 RNA	X	X	X	X	X[n]	X[n]	X[n]		X[n]	X	
Lymphocyte subset	X	X	X	X	X	X	X		X	X	X
Plasma for storage[e]	X	X	X	X	X	X	X		X	X	X
HLA-B* 5701 testing[q]	X										
Clinical chemistry	X	X	X	X	X	X	X		X	X	X
Hematology	X	X	X	X	X	X	X		X	X	X
Fasting lipids and glucose[f]		X		X	X	X	X				
Urinalysis and spot urine for protein analysis[g]		X			X		X		X[p]	X[m]	X
Pregnancy test[h]	S	U	S	S	S	S	S		S	S	
HBsAg and hepatitis C antibody	X										
Pharmacogenetic sample[i]		X									
Bone marker analytes (blood)[v]		X			X		X				
Investigational Product											
IVRS	X	X	X	X	X	X	X		X	X	X
Dispense IP		X	X	X	X	X	X[o]		X		
IP accountability (pill counts)			X	X	X	X	X		X	X	

a. The 14-day Screening period maybe extended to 28 days. Randomization may occur as soon as all Screening results are available.
b. Inclusion/exclusion criteria will be fully assessed at the Screening visit. Changes between the screening visit and the Day 1 visit should be assessed to ensure eligibility, including additional assessments performed at Day 1.
c. Full medical history will be collected. Targeted medical history assessments will include cardiovascular, metabolic (e.g., Type I or II DM), psychiatric (e.g, depression) and renal (e.g., nephrolithiasis, nephropathy, renal failure) disorders.
d. Assessment for cardiovascular risk will include height, weight, blood pressure, smoking history, medical conditions, and family history of premature cardiovascular disease
e. Plasma samples for storage will be collected at each visit for possible future analyses (including but not limited to HIV-1 RNA genotypic and phenotypic analyses, HIV-1 RNA levels, and immunological parameters). These samples will be used when needed such as when samples are lost or arrive at the laboratory unevaluable. Additionally, these samples will be used for genotypic and/or phenotypic analyses when subjects meet confirmed virologic withdrawal criteria.

f. An overnight fast is preferred, however a minimum of a 6 hour fast is acceptable.
g. A morning specimen is preferred.
h. Pregnancy testing. Women of childbearing potential only. S=serum, U=urine. Remind females of reproductive potential of the need to avoid pregnancy while in study and adherence to the study's contraception requirements.
i. Informed consent for optional pharmacogenetics (PGx) research must be obtained before collecting a sample. Collection of the PGx sample at Day 1 is preferred, however this sample may be collected at any time during the study.
j. Only SAEs related to study participation or to a concomitantly administered GSK product will be collected between obtaining informed consent and administration of IP at Day 1.
k. For subjects who completed randomized DTG/ABC/3TC FDC through Week 48 and entered into DTG/ABC/3TC FDC Continuation Phase: subjects completing the DTG/ABC/3TC FDC Continuation Phase must return to the clinic when transitioning to commercial supplies. Conduct study assessments as specified per the Week 36 schedule at this end of Continuation Phase visit.
l. A Follow up visit may be conducted approximately 4 weeks after the last dose of study provided IP, and is required only if the subject has ongoing AEs or lab abnormalities at the last on study visit. The assessments performed should reflect what is considered medically necessary to assess the event(s).
m. Conduct assessments at Week 48 OR at the Withdrawal visit for subjects who discontinue from the study prior to Week 48, but not both.
n. Beginning at Week 24, subjects with plasma HIV-1 RNA ≥50 but <400 c/mL who elect to remain in study must return every 4-6 weeks for collection of samples for HIV-1 RNA determination and plasma for storage. Genotype and phenotype testing will only be performed with confirmed HIV-1 RNA ≥400 c/mL.
o. For subjects receiving DTG/ABC/3TC FDC in Continuation Phase only
p. Will be tested every 24 weeks (not every 12 weeks)
q. Documentation that the subject had been screened for, and is negative for the HLA-B*5701 allele is acceptable.
r. Contacts at Week 8,18, 30 and 42 are mandatory but may be conducted as a telephone, clinic or home visit (or other type of visit as agreed with GSK).
s. Limited physical examination to include blood pressure at Baseline (recorded in eCRF) for Framingham score assessment, and weight at each visit (recorded in eCRF at Baseline and on lab requisition at all visits) for determination of CrCL. Blood pressure to be measured after resting in a semi-supine position for at least 5 minutes.
t. A 12-lead electrocardiograph (ECG) will be performed after resting in a semi-supine position for at least 5 minutes.
u. On Day 1, the Columbia Suicidality Severity Rating Scale (conducted by voice response system) is to be administered **prior to** randomization.
v. Blood sample for bone marker assessment. Only the result for 25 hydroxy-vitamin D will be reported to the investigator.
w. SF-12 and HIV Treatment Satisfaction Questionnaire **(**HIVTSQ) is recommended to be administered at the beginning of the visit.

12.3. Appendix 3: Assessment Windows

Laboratory data, vital signs, ECGs, health outcomes assessments, 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. The CVW algorithm will be derived using nominal CRF visit rather than using the assessment window defined below.

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.

12.3.1. Definitions of Assessment Windows for Analyses

Analysis Set / Domain	Parameter (if applicable)	Target	Analysis Window		Analysis Timepoint
			Beginning Timepoint	Ending Timepoint	
All	All	-28	<=-4	<=-4	Screening
		1	-3	1	Day 1
		29	2	56	Week 4
		85	57	126	Week 12
		169	127	210	Week 24
		253	211	294	Week 36
		337	295	Date of Week 48 visit	Week 48
		421	Date of Week 48 visit +1	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)	-	Follow-up

1. **NOTES :**

- For parameters which are not scheduled to be assessed at particular visits, the all- inclusive windows defined will still be used.
- Data summaries will only report scheduled visits. 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).

1.

12.4. Appendix 4: Treatment States & Phases

12.4.1. Treatment Phases

All displays are for the randomised phase only, unless specified otherwise.

Data collected from both arms up to and including the date of the Week 48 visit, or unscheduled Week 48 visit date, will be considered to be during the Randomised Phase of the Study.

Data collected from the DTG/ABC/3TC FDC arm after Week 48, or unscheduled Week 48 visit, to the end of the study will be considered to be during the Continuation Phase of the Study.

12.4.2. Treatment States

Assessments and events will be classified according to time of occurrence relative to the start and/or stop date of the study treatment.

12.4.2.1. Treatment States for Laboratory, HIV Associated Conditions, Vital Signs, ECGs, Health Outcomes and Genotypic and Phenotypic Data

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

1. **NOTES:**

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

12.4.2.2. Treatment States for AE Data

For adverse events, partial AE start date will use imputation as described in Section 12.7.2.1. 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.

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

NOTES:

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

12.4.2.3. Treatment States for Prior/Concomitant/Post-Therapy Medications Data

- Prior medications: Those taken (i.e., started) before the start date of investigational product.

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

- Post treatment medications: Those started after the stop date of study treatment. Concomitant medications that were continued during this period are also considered as post-treatment medications.

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

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

- ART starting on study treatment stop date will be considered as only post-treatment and not concomitant. It is expected that after discontinuation of study treatment, a subject may immediately begin taking another ART.

- ART stopping on study treatment start date will only be considered as prior and not concomitant.

- Any ART entered on the Prior ART eCRF with partial end date will be assumed to have finished before Screeninig.

	Pre-treatment	On-treatment			Post-treatment		Prior	Conco-mitant	Post
		IP Start Date		IP Stop Date	IP Stop Date+1				
(a)	x————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

1. x = start/stop date of medication
2. ? = missing start/stop date of medication
3. * 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
4. ** 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
5. *** 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

12.4.3. Treatment Phases and States

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

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

12.5. Appendix 5: Data Display Standards & Handling Conventions

12.5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order [1]
A	DTG/ABC/3TC FDC once daily	DTG/ABC/3TC	1
B	ATV +RTV +TDF/FTC FDC once daily	ATV +RTV +TDF/FTC	2

NOTES:

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

12.5.2. Baseline Definition & Derivations

12.5.2.1. Baseline Definitions

For all endpoints (unless stated otherwise) the baseline value will be the latest pre-dose assessment. 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.

12.5.2.2. Derivations and Handling of Missing Baseline Data

Definition	Reporting Details
Change from Baseline	= Post-Dose Visit Value – Baseline
% Change from Baseline	= 100 x [(Post-Dose Visit Value – Baseline) / Baseline]
Maximum Change from Baseline	= Calculate the change from baseline at each given timepoint and determine the maximum change

NOTES :

- Unless otherwise specified, the baseline definitions specified in Section 12.5.2.1 Baseline Definitions will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.

12.5.3. Reporting Process & Standards

Reporting Process	
Software	
• The currently supported versions of SAS software and TSCG will be used.	
Reporting Area	
HARP Server	: uk1salx00175
HARP Area	: \ARPROD\GSK2619619\ING117172
QC Spreadsheet	: \ARPROD\ GSK2619619\ING117172\(Week48 or Final)\Documents
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.1.3 &	

Reporting Process
AdaM IG Version 1.0. • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM.
Generation of RTF Files
• RTF files will be generated for the Week 48 and end of study 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
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) 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 DP's.
Planned and Actual Time
• Reporting for tables, figures and formal statistical analyses : • Actual time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated. • 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 or unplanned readings will be presented within the subject's listings. • Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures, summaries and statistical analyses.
Unscheduled Visits
• Unscheduled visits will be assigned to a study visit using the all-inclusive windows defined in Section 12.3.1. • However, data summaries will only report visits that are planned assessment time points for each parameter (according to the T&E 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).

Reporting Standards	
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.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

12.6. Appendix 6: Derived and Transformed Data

12.6.1. General

Multiple Measurements at One Time Point
• If after window assignment there are multiple valid (see Section 12.3) assessments of a parameter within the same window, then the following hierarchy will be used to determine the value to be used for summary statistics of observed values: o the assessment closest to the window target Study Day; o if there are multiple assessments equidistant from the target Study Day, then the mean of these values will be used. For HIV-1 RNA, the geometric mean of the number of copies will be used as opposed to the arithmetic mean • Assessments not chosen for use in summary statistics by this algorithm will still appear in the associated listings. Also, such valid assessments will be used when determining values of potential clinical concern for the 'any time On-treatment' time point, and for any algorithm that has specific rules for which observation to use (e.g., SNAPSHOT or LOCF).
Study Day
• Calculated as the number of days from initial study treatment start date : • Ref Date = Missing → Study Day = Missing • Ref Date < Treatment Start Date → Study Day = Ref Date –Treatment Start Date • Ref Data ≥ Treatment Start Date → Study Day = Ref Date – (Treatment Start Date) + 1 Note that Treatment Start Date is considered to be on Study Day 1 and the day before this is Study Day -1; i.e., there is no Study Day 0.
Post-baseline
• Post-baseline refers to the combined time periods of On-treatment and Post-treatment. Post-baseline may be further specified according to phase of the study: Randomized or Continuation.

12.6.2. Study Population

Demographics

Age

- Age, in whole years, will be calculated with respect to the subject's Screening visit.
- GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
  - Any subject with a missing day will have this imputed as day '15'.
  - Any subject with a missing date and month will have this imputed as '30th June'.
- 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)

- Calculated as **Weight (kg) / Height (m)^2**

Hepatitis Status

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

Framingham Risk Equation

- The predicted probability, p, for time (t = 4,...,12 years) of coronary heart disease according to the Framingham equation [Anderson, 1991] is :

$$p = 1 - \exp\left(-\mathrm{e}^{u}\right)$$

where

$$u = \frac{\log(t) - \mu}{\sigma}$$

with

$$\mu = 4.4181 + m$$

and

$$\sigma = \exp(-0.3155 - 0.2784 \times m)$$

- The quantity m is calculated as

$$m = \begin{cases} a - 1.4792 \times \log(age) - 0.1759 \times I_d & \text{if male} \\ a - 5.8549 + 1.8515 \times \left[\log(age/74)\right]^2 - 0.3758 \times I_d & \text{if female} \end{cases}$$

where

Demographics

$$a = 11.1122 - 0.9119 \times \log(SBP) - 0.2767 \times I_s - 0.7181 \times \log(TC / HDL) - 0.5865 \times I_{LVH}$$

and

$$I_d = \begin{cases} 1 & \text{if diabetic subject} \\ 0 & \text{otherwise} \end{cases}$$

$$I_s = \begin{cases} 1 & \text{current or former smoker} \\ 0 & \text{otherwise} \end{cases}$$

SBP = systolic blood pressure (mmHg)

TC = total serum cholesterol

HDL = serum HDL cholesterol

$$I_{LVH} = \begin{cases} 1 & \text{definite ECG for left ventricular hypertrophy} \\ 0 & \text{otherwise} \end{cases}$$

with total cholesterol and HDL cholesterol measured in the same units.

- A subject is classified as diabetic if current or past is indicated in the medical conditions eCRF for Type 1 or Type 2 diabetes mellitus, or if baseline fasting glucose ≥7.00 mmol/L (126 mg/dL).
- Smoking status is collected in the eCRF on Day 1. A current smoker is defined as currently smoking/using tobacco or has smoked/used tobacco within the previous 6 months; a former smoker is defined as previously smoked/used tobacco products and has not smoked/used tobacco products within the previous 6 months.
- Definite ECG for left ventricular hypertrophy (LVH) is assessed based on current or past indication in the medical conditions eCRF for LVH.
- This calculation will not be performed for subjects who have indicated current or past myocardial infarction conditions on the eCRF. These subjects will not be included in summary statistics of risk, but will be counted in the highest category of risk in the summary by category.

Extent of Exposure

- Number of days of exposure to study drug will be calculated based on the formula:
  Duration of Exposure in Days = Treatment Stop Date – (Treatment Start Date) + 1
- In the situation where IP consists of more than one drug, the earliest start date and latest stop date will be used.
- Subjects who were randomized but did not report a treatment start date will be categorised as having zero days of exposure.
- Missing Treatment Stop Date will be imputed, for purposes of calculating exposure, as the date of last visit or the recorded date of withdrawal/completion, whichever is earlier.
- An alternative calculation of exposure will be performed where the duration of any dosing interruptions based on eCRF data will be subtracted from the result above.
  - The ratio (percentage) of the actual exposure to the overall exposure (i.e. study

Extent of Exposure
treatment stop date – study treatment start date+1) will be used to define protocol deviation leading to exclusion from PP Population due to study treatment interruption (i.e. >10%). ○ Due to local supply issues of RTV during the study, some subjects had to take locally prescribed RTV and this is reported on the CONEMDS eCRF rather than IP eCRF. When calculating interruptions, RTV records on the CONMEDS eCRF will be used in conjunction with the IP eCRF data.

12.6.3. Safety

ECG Parameters
RR Interval
• IF RR interval (msec) is not provided directly, then RR can be derived as : [1] If QTcB is machine read & QTcF is not provided, then : $$RR = \left[\left(\frac{QT}{QTcB}\right)^2\right] * 1000$$ [2] If QTcF is machine read and QTcB is not provided, then: $$RR = \left[\left(\frac{QT}{QTcF}\right)^3\right] * 1000$$ • If ECGs are manually read, the RR value preceding the measurement QT interval should be a collected value THEN do not derive.
Corrected QT Intervals
• When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fredericia's (QTcF) formulas will be calculated, in msec, depending on the availability of other measurements. • IF RR interval (msec) is provided then missing QTcB and/or QTcF will be derived as : $$QTcB = \frac{QT}{\sqrt{\frac{RR}{1000}}} \qquad QTcF = \frac{QT}{\sqrt[3]{\frac{RR}{1000}}}$$

Adverse Events
AE Severity – DAIDS Grading
• The DAIDS grading for severity of clinical adverse events will be performed. • See protocol for DAIDS grading criteria.

Laboratory Parameters
• 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.

Laboratory Parameters

- 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

Glomerular Filtration Rate (GFR)

- The Cockroft-Gault method will be used by the central laboratory to provide an estimate of GFR, in mL/min, as follows:

$$\mathrm{GFR} = \frac{(140 - \mathrm{age}) \times \mathrm{weight} \times 88.4}{\mathrm{CRT}_{\mu\mathrm{mol/L}} \times 72} \times (0.85 \text{ if female})$$

$$= \frac{(140 - \mathrm{age}) \times \mathrm{weight}}{\mathrm{CRT}_{\mathrm{mg/dL}} \times 72} \times (0.85 \text{ if female})$$

where age (in years) and weight (in kg) are at time of assessment, and CRTμmol/L is serum creatinine concentration in GSK standard units of μmol/L. CRTmg/dL is serum creatinine concentration in mg/dL, and CRTμmol/L=88.4x CRTmg/dL.

Lab Toxicities – DAIDS Grading

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

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

National Cholesterol Education Program (NCEP) Lipid Categories

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

Parameter	Value Range (mmol/L)	Value Range (mg/dL)	Category
Triglycerides	<1.70	<150	Normal
	1.70 to <2.26	150 to <200	Borderline High
	2.26 to <5.65	200 to <500	High
	≥5.65	≥500	Very High
Total Cholesterol	<5.18	<200	Desirable
	5.18 to <6.21	200 to <240	Borderline High
	≥6.21	≥240	High
HDL Cholesterol	<1.04	<40	Low

Laboratory Parameters

	1.04 to <1.56	40 to <60	Normal
	≥1.56	≥60	High
LDL Cholesterol	<2.59	<100	Optimal
	2.59 to <3.37	100 to <130	Near/Above Optimal
	3.37 to <4.14	130 to <160	Borderline High
	4.14 to <4.92	160 to <190	High
	≥4.92	≥190	Very High

Total Cholesterol / HDL Cholesterol Ratio

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

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

Other Safety Endpoints

Columbia Suicide Severity Rating Scale (C-SSRS)

- Missing data will not have any imputation performed.
- Incomplete calls:
  - when no complete call is databased on the same day, the incomplete data will be used
  - 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, the latest entry will be used.
  - If they occur on different days, take the entry closest to the target visit date.

12.6.4. Efficacy

HIV-1 RNA

Snapshot (Missing, Switch or Discontinuation=Failure)

- It is intended to be primarily a virologic assessment of the endpoint, and as such follows a "virology first" hierarchy.
- Virologic Success (e.g., <50 c/mL) or Virologic Failure within an analysis window (see Section 12.3.1) 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 a Virologic

HIV-1 RNA

Success. Depending on the reason for lack of data, the subject will be classified as a Virologic Failure or reported as 'No Virologic Data at Week X'; in the latter case, the algorithm further classifies the nature of the missing data. Typically, a subject withdrawn (i) due to AE or, (ii) for another reason yet was suppressed at the time, will be counted as 'No Virologic Data at Week X'. Should a subject withdraw for reasons other than AE and was not suppressed at the time, they will be a Virologic Failure.

- For each scheduled assessment time, the snapshot response rate for a given threshold (e.g., <50 c/mL) is defined as:

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

- Full details of the algorithm, including the handling of special cases, are included in Section 12.11

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.

Treatment (TRDF) and Efficacy Related (ERDF) Discontinuation = Failure

- The analysis of time to Confirmed Virologic Withdrawal or discontinuation due to treatment related reasons (i.e., drug-related AE, protocol defined safety stopping criteria, or lack of efficacy) will censor subjects who have not met CVW criteria and are ongoing in the study, or who have discontinued for reasons other than those related to treatment. This will be the Treatment Related Discontinuation = Failure (TRDF) data.
- Subjects who have not met CVW criteria and are ongoing in the study, or who have discontinued for reasons other than lack of efficacy, will be censored in the analysis of the Efficacy Related Discontinuation = Failure (ERDF) data.

Variance Estimator of Cochran Mantel-Haenszel Risk Difference

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

where

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

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

12.6.5. Viral Genotyping and Phenotyping

Genotype

Amino Acid Changes

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

Representation of Amino Acid Changes

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

A mutation as treatment emergent in class XX, the subject must have received a drug YY in class XX as part of their study treatment, and the mutation must be associated with resistance to a drug in class XX and not present at baseline.

Resistance Associated Mutations

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

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

NOTES:

- Draft listing; may be modified in case of additional substantive data availability.
- INI mutations listed taken from Stanford HIV Resistance Database (http://hivdb.stanford.edu/DR/cgi-bin/rules_scores_hivdb.cgi?class=INI cited 28 Feb 2014) and accessed on 16 Feb 2015.
- Each INI mutation listed had a score of ≥15. 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

Genotype

Amino Acid Changes

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.

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, Q58E, T74P, L76V, V82A/T/F/L/S, N83D, I84V, N88S,L90M

Note: List generated from IAS_USA Guideline, [Wensing, 2014]

Phenotype

Phenotypic Susceptibility

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

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

Drug	Abbreviation	Class	PhenoSense cutoff
Abacavir	ABC	NRTI	(4.5 – 6.5)[a]
Lamivudine	3TC	NRTI	3.5[a]
Didanosine	ddI	NRTI	(1.3 – 2.2)[a]
Stavudine	d4T	NRTI	1.7[a]
Zidovudine	AZT (ZDV)	NRTI	1.9
Emtricitabine	FTC	NRTI	3.5
Tenofovir	TDF	NRTI	(1.4 – 4)[a]
Delavirdine	DLV	NNRTI	6.2
Efavirenz	EFV	NNRTI	3

Phenotype			
Nevirapine	NVP	NNRTI	4.5
Etravirine	ETR	NNRTI	(2.9-10) [a]
Rilpivarine	RPV	NNRTI	2
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]

a. clinical cutoff (lower cutoff – higher cutoff)

12.6.6. Health outcomes

HIVTSQs

Treatment Satisfaction Total Score

- Items 1 to 10 are summed to produce a score with a possible range of 0 to 60.
- Higher scores represent greater treatment satisfaction as compared to the past few weeks.
- A maximum of 5 items can be missing, which can be imputed to reflect the mean of the completed item scores. If 6 or more items are missing, then the overall treatment satisfaction scale score should not be computed and will remain missing.

General Satisfaction/Clinical Sub-Score

- Items 1, 2, 3, 9, and 10 are summed to produce a score with a possible range of 0 to 30.
- Higher scores represent greater treatment satisfaction within this subscale as compared to the past few weeks.
- These subscales can be computed if at least 4 out of 5 items are available, in which case, the missing item can be imputed to reflect the mean of the completed item scores. If 2 or more items are missing, the score should not be computed and remain missing.

Lifestyle/Ease Sub-Score

- Items 4, 5, 6, 7, and 8 are summed to produce a score with a possible range of 0 to 30.
- Higher scores represent greater treatment satisfaction within this subscale as compared to the past few weeks.
- These subscales can be computed if at least 4 out of 5 items are available, in which case, the missing item can be imputed to reflect the mean of the completed item scores. If 2 or more items are missing, the score should not be computed and remain missing.

Individual Item Scores

- Items are rated as 6 (very satisfied, convenient, flexible, etc.) to 0 (very dissatisfied,

inconvenient, inflexible, etc.). • Higher scores represent greater satisfaction with each aspect of treatment. • Missing scores will not be computed and should remain missing.

SF-12
Physical Component Score (PCS) and Mental Component Score (MCS)
• Scores are created according to the manual [Ware, 1996] and are scored using software purchased from Quality Metric http://www.qualitymetric.com/.

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

12.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as: o Randomized to ATV+RTV+TDF/FTC FDC and completed the Randomized Phase including the Week 48 Study Visit; o Randomized to DTG/ABC/3TC FDC, completed the Randomized Phase including the Week 48 Visit, and did not enter the Continuation Phase; o Randomized to DTG/ABC/3TC FDC, completed the Randomized Phase, including the Week 48 study visit, entered and completed the Continuation Phase (defined as remaining on study until commercial supplies of DTG/ABC/3TC become locally available or development of DTG/ABC/3TC is terminated). • Withdrawn subjects were not replaced in the study. • All available data from subjects who were withdrawn from the study will be listed.

12.7.2. 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. o Answers such as “Not applicable” and “Not evaluable” are not considered to be missing data and should be displayed as such. • Unless stated, no imputation for missing data or premature discontinuation will be performed and the observed values will be used.
Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.
Health Outcomes HIV TSQ	• For the HIV Treatment Satisfaction overall score (which is comprised of all 10 items), a maximum of 5 items may be missed and each computed as the mean of the completed item scores (as discussed in [Woodcock, 2006; Woodcock, 2001 o If 6 or more items are missed, then the overall score should not be computed and instead be imputed using LOCF. • For the lifestyle/ease sub-score (which is comprised of 5 items), a maximum of 1 item may be missed and computed as the mean of the completed item scores. o If 2 or more items are missed, then the overall score should not be computed and instead be imputed using LOCF. • For the convenience item and other individual item scores, missing scores will not be computed (according to Page 7 of the [HIVTSQ User Guidelines]) and

Element	Reporting Detail
	instead be imputed using LOCF.

12.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.
Exposure	If study treatment stop date is missing, then for the purposes of calculating exposure, it will be imputed using the date of last visit or the recorded date of withdrawal/completion whichever is earlier.
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. • Any partial dates for adverse events will be raised to data management. • If the full date cannot be ascertained, the following assumptions will be made: 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, 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 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, 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. • The recorded partial date will be displayed in listings.
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 o 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.

12.7.2.2. Handling of Missing Data for Statistical Analysis

Element	Reporting Detail
Snapshot	• In the Snapshot dataset, subjects without HIV-1 RNA data in the assessment window for the visit of interest (due to missing data or discontinuation of IP prior to the visit window) are classified as non-responders in the derivation of the proportion of subjects with HIV-1 RNA < 50 c/mL (or <400 c/mL). The nature of this missing data will be further classified in Snapshot summaries as either 'Virologic Failure' or 'No Virologic Data at Week X'; see Section 12.11 for full details
LOCF	• In the LOCF dataset, missing values will be carried forward from the previous, non-missing available on-treatment assessment.
Lipid LOCF	• If subjects initiate serum lipid-lowering agents Post-baseline, then the last available fasted On-treatment lipid values prior to the initiation will be used in place of future, observed On-treatment values. • Imputation will continue even if the subject discontinues the lipid-lowering agent. • Missing assessments will not be imputed. Subjects on lipid-lowering agents at baseline will be excluded from this dataset. • This dataset will be used for all summaries of lipids data.

12.8. Appendix 8: Values of Potential Clinical Importance

Element	Reporting Detail
Laboratory Values and Adverse Events	• The DAIDS grading for severity of laboratory toxicities and clinical adverse events is included in the protocol. • The central laboratory will flag lab parameter toxicities directly in the provided datasets.
ECG	• QTc above 500 msec or change from baseline above 60 msec are considered to be values of potential clinical importance.

12.9. Appendix 9: Examination of Covariates and Subgroups

12.9.1. Handling of Covariates, Subgroups & Other Strata

- The following is a list of covariates that may be used in descriptive summaries and statistical analyses, some of which may also be used for subgroup analyses (See Section 9.1.1 for further details).
- Additional covariates of clinical interest may also be considered.
- If the percentage of subjects is small within a particular subgroup, then the subgroup categories may be refined prior to unblinding the trial.
- If the category cannot be refined further, then descriptive rather than statistical comparisons may be performed for the particular subgroup.

Category	Covariates and / or Subgroups
Randomisation Strata	Randomisation is stratified by screening plasma HIV-1 RNA and CD4+ cell count, although summaries and analyses will make use of the Baseline categories, which are considered to be more relevant to the analysis of the study endpoints: • Baseline plasma HIV-1 RNA (≤ vs. >100,000 c/mL) • Baseline CD4+ cell count (≤ vs. >350 cells/mm^3). All statistical analyses will adjust for the above randomization strata, unless stated otherwise. Treatment-by-Strata interactions will be assessed as specified in the analysis sections.

Demographic and Baseline Characteristic Subgroups	• Age: ≥50 & <50
	• Race:
	  ○ White; Non-White
	  ○ African American/African Heritage; Non-African American/African Heritage
	• Country
	• Baseline plasma HIV-1 RNA:
	  ○ <1000; 1000 to <10,000; 10,000 to <50,000; 50,000 to 100,000; >100,000 c/mL.
	• Baseline CD4+ cell count:
	  ○ <50; 50 to <200; 200 to <350; 350 to <500; ≥500 cells/mm3.
	• Baseline Centers for Disease Control and Prevention (CDC) category:
	  ○ CDC Category A,
	  ○ CDC Category B
	  ○ CDC Category C;
	• HIV-1 Subtype: B vs non-B.

12.10. Appendix 10: Model Checking and Diagnostics for Statistical Analyses

12.10.1. Statistical Analysis Assumptions

Endpoint(s)	Change from Baseline in fasted lipids (triglycerides and TC/HDL ratio)
Analysis	Multiple imputation

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

Analysis	MMRM

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

12.11. Appendix 11: Snapshot

Detailed Algorithm Steps

- Consider an arbitrary visit window, Week X (see Section 12.3).
- A subject's response (i.e., 'Virologic Success', 'Virologic Failure', or 'No Virologic Data at Week X') in that window is determined as indicated below, in the order stated.

1. If non-permitted change in background ART **prior** to Week X: Subject = Virologic Failure.
2. If permitted change in background ART **prior** to Week X AND decision to make this change is *after* the first On-treatment HIV-1 RNA result AND the latest On-treatment HIV-1 RNA result prior to the date of decision to switch is ≥ 50 c/mL: Subject = Virologic Failure.
3. If non-permitted change in background ART **during** Week X

   OR

   if permitted change in background ART **during** Week X AND decision to make this change is *after* the first On-treatment HIV-1 RNA result AND the latest On-treatment HIV-1 RNA result prior to the date of decision to switch is >=50 c/mL

   AND:

   - no HIV-1 RNA result is available during Week X prior to change: Subject = Virologic Failure;
   - there is at least one HIV-1 RNA result available during Week X prior to the change, then consider the latest such result:
     - If < 50 c/mL: Subject = Virologic Success
     - If ≥ 50 c/mL: Subject = Virologic Failure.
4. If there is no change in background ART **prior or during** Week X

   OR

   a permitted change **prior or during** Week X is decided on *before* the first On-treatment HIV-1 RNA result,

   OR

   a permitted change **prior or during** Week X is decided on *after* the first On-treatment RNA result AND the latest On-treatment HIV-1 RNA result prior to the decision to switch is <50 c/mL,

   AND

   at least one HIV-1 RNA result is available during Week X, then consider the latest such result:

   - If < 50 c/mL: Subject = Virologic Success;
   - If ≥ 50 c/mL: Subject = Virologic Failure.
5. If there is no change in background ART **prior or during** Week X

   OR

   a permitted change **prior or during** Week X is decided on *before* the first On-treatment HIV-1 RNA result

Detailed Algorithm Steps

OR

a permitted change **prior or during** Week X is decided on *after* the first On-treatment RNA result AND the latest On-treatment HIV-1 RNA result prior to the decision to switch is <50 c/mL,

AND

no HIV-1 RNA results are available during Week X:

- If the subject has not withdrawn from the study prior to or during Week X: Subject = No Virologic Data at Week X, with a reason of 'Missing data during window but on study';
- If the subject was withdrawn from the study prior to or during Week X due to AE or death: Subject = No Virologic Data at Week X, with a reason of 'Discontinued due to AE or Death';
- Otherwise, consider the subject's last available On-treatment HIV-1 RNA result:
  - If <50 c/mL or no result is available: Subject = No Virologic Data at Week X, with a reason of 'Discontinued for Other Reasons';
  - If ≥ 50 c/mL: Subject = Virologic Failure.

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 copies/mL at Day 336, HIV-RNA below 50 copies/mL on Day 350. This should be categorized as Virologic Success.

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 copies/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 copies/mL at Day 336 and discontinues because of AE or even dies on Day 360 — this person is categorized as Virologic Success.
  b. HIV-RNA is 552 copies/mL on Day 336 and the patient discontinues on Day 360, the patient is categorized as Virologic Failure.

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 Virologic Failure row and not in the Discontinued for

Detailed Algorithm Steps
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 copies/mL, then he or she should be categorized as Virologic Failure 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 copies/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 as Virologic Failure. On study but missing data in window: • If there are no data during Days 295 to 378, but there is an HIV-RNA below 50 copies/mL on Day 380, this patient should be considered *On Study but Missing Data in Window.* • If there are no data during Days 295 to 378, but there is an HIV-RNA equal to or above 50 copies/mL on Day 280, this patient also should be classified as *On Study but Missing Data in Window.* Optimized Background Therapy Substitutions After Randomization • 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 Virologic Failure if they have HIV-RNA above 50 copies/mL at the time of switch.

12.12. Appendix 12: Abbreviations & Trade Marks

12.12.1. Abbreviations

Abbreviation	Description
ABC	Abacavir
ADaM	Analysis Data Model
AE	Adverse Event
ALT	Alanine aminotransferase
ART	Antiretroviral Treatment
ATC	Anatomical Therapeutic Chemical
ATV	Atazanavir
c/ml	Copies per milliliter
CDC	Centers for Disease Control and Prevention
CDISC	Clinical Data Interchange Standards Consortium
CD4+	Helper-inducer T-lymphocyte having surface antigen CD4 (cluster of differentiation 4)
CI	Confidence Interval
CMH	Cochran-Mantel-Haenszel
CRT	Serum creatinine
CSR	Clinical Study Report
C-SSRS	Columbia Suicide Severity Rating Scale
CV	Cardiovascular
DAIDS	Division of AIDS
DP	Decimal Places
ECG	Electrocardiogram
eCRF	Electronic Case Record Form
ERDF	Efficacy Related Discontinuation = Failure
FC	Fold change
FDA	Food and Drug Agency
FDC	Fixed Dose Combination
FU	Follow-up
GFR	Glomerular Filtration Rate
GSK	GlaxoSmithKline
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HDL	High density lipoprotein
HIV(-1)	Human immunodeficiency virus (type 1)
HIVTSQs	HIV Treatment Satisfaction Questionnaire
HSR	Hypersensitivity reaction
IAS-USA	International Antiviral Society-USA
ICH	International Conference on Harmonisation
IDSL	Integrated Data Standards Library
IG	Implementation Guide
IN(I)	Integrase (Inhibitor)
IP	Investigational Product

Abbreviation	Description
ITT(E)	Intent-To-Treat (Exposed)
LDL	Low density lipoprotein
LOCF	Last Observation Carries Forward
LVH	left ventricular hypertrophy
MAR	Missing at random
MCMC	Markov Chain Monte Carlo
MCS	Mental Component Score
MedDRA	Medical Dictionary for Regulatory Activities
MI	Multiple Imputation
MMRM	Mixed Model Repeated Measures
NCEP	National Cholesterol Education Program
NNRTI	Non-nucleoside Reverse Transcript Inhibitor
NRTI	Nucleoside Reverse Transcript Inhibitor
OC	Observed Case
PCS	Physical Component Score
PDMP	Protocol Deviation Management Plan
PI	Protease Inhibitor
PP	Per Protocol
PSRAE	Possibly suicidality related Adverse Event
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RAMOS	Randomization & Medication Ordering System
RNA	Ribonucleic acid
RTF	Rich text format
RTV	Ritonavir
RUCAM	Roussel Uclaf Causality Assessment Method
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SAS	Statistical Analysis Software
SBP	Systolic blood pressure
SDTM	Study Data Tabulation Model
SF-12	12-Item Short Form
SOC	System Organ Class
TC	Total Cholesterol
TDF/FTC	Tenofovir/emtricitabine
TFL	Tables, Figures & Listings
TRDF	Treatment Related Discontinuation = Failure
VF	Virologic Failure

12.12.2. Trademarks

Trademarks of ViiV Healthcare
Dolutegravir
Epzicom/Kivexa

Trademarks not owned by ViiV Healthcare
Norvir
Reyataz
SAS
Truvada
TSCG
TYLENOL

12.13. Appendix 13: Final (End of Study) Analysis

This appendix provides the details of the planned analyses and data displays for ING117172 End of Study (EoS) reporting.

The primary analysis (i.e. interim analysis at Week 48) was completed based on the original RAP. This appendix is written to cover only analyses included in the final end of study reporting. All derivations described in the study analysis plan will be re-used for end of study reporting and only those definitions and derivations that have changed since the previous interim analysis are described below. This additional appendix summarizes only the key endpoints of interest for the final analysis and explain any deviations from the primary analysis. The details of the final EOS reporting and analysis plan are described below:

1. The analysis for which the data have not been changed since last interim analysis will not be reported to avoid redundancy. These reports include the analyses of demographic and baseline characteristics.
2. No subgroup analysis, hypotheses testing, or statistical analyses will be performed.
3. All required disclosure outputs following the FDAAA and EudraCT guidelines will be produced.
4. For the purpose of creation of Mexico Final Safety Report and submission to Ministry of Health, some listings at Mexico sites will be reported separately. Such listings are identified in the Programming notes in Section 12.13.8. These listings will include data from both Randomized and Continuation Phase.
5. All by visit tables will have all visits reported from both Randomized and Continuation Phase.
6. All listings that include both Randomized and Continuation Phase data will have the Phase mentioned in the outputs except for Listing of Investigational Product Exposure Data.

12.13.1. Study Phases

In previous analysis (primary Week 48 reporting), data were summarized only for the Randomized phase of the study. However, when data from the Continuation phase were available, certain displays were repeated for the combined time period of Randomized plus Continuation phases. For EoS reporting, if for any display, data from both study phases (Randomized phase plus Continuation phase) are included, they will be tabulated in one summary table, unless specified otherwise, and it will be noted in the title of the output. For listings that contain all the data, a new column will be added to specify the phase of the study for each record.

Start and end date for Randomized and open-label phases are defined as follows:

Study Treatment Date	**Definition**
Randomized phase treatment start date	The earliest exposure start date, where investigational product is either DTG/ABC/3TC or ATV+RTV+TDF/FTC
Randomized phase treatment end date	• If Treatment arm= ATV+RTV+TDF/FTC ▪ Randomized phase treatment end date= Last non-missing exposure date. • If Treatment arm= DTG/ABC/3TC ▪ Randomized phase treatment end date= Week 48 visit date or unscheduled Week 48 visit date. ▪ If the participant discontinued the study before Week 48, then Randomized phase treatment end date= Last non-missing exposure end date
Continuation phase treatment start date	• Randomization phase treatment end date+1 day where Treatment arm = DTG/ABC/3TC • There will be no Continuation phase if Treatment arm= ATV+RTV+TDF/FTC.
Continuation phase treatment end date	• The last non-missing exposure end date after entering the Continuation Phase in the DTG/ABC/3TC arm.

12.13.1.1. Study Phases for all events that do not have visits associated with them

Phase	Definition
Randomized Phase Event	Randomized phase treatment start date ≤ Event Start Date ≤Randomized phase end date
Continuation Phase Event	Event Start Date ≥ Continuation phase treatment start date

- Note: In the case of a completely missing start date, the event will be considered to have started in the Randomized Phase.

12.13.1.2. Treatment Phases for Concomitant/Post-Therapy Medications Data

- For subjects who do not enter into Continuation phase, all on-treatment and post-treatment concomitant medications (conmeds) will be in Randomized phase;
- For subjects who enter into Continuation phase; all on-treatment and post-treatment conmeds will be in Randomized phase, Continuation phase or both (Randomized + Continuation) phases depending on the conmeds start/stop dates.
    - Randomized phase- If the conmeds end dates <Continuation treatment start date.
    - Continuation phase- If the conmeds start dates ≥Continuation treatment start date.
    - Randomized and Continuation-
        - If conmed start date< Continuation treatment start date + conmed end date≥ Continuation treatment start date
        - If conmed start date< Continuation treatment start date + conmed end date= missing
        - If conmed start date= missing + conmed end date≥ Continuation treatment start date
        - If conmed start date= missing + conmed end date= missing

12.13.2. Analysis Populations for the Continuation Phase

The following populations have been defined only for the Continuation Phase. For all other populations refer to Section 5.

Population	Definition/ Criteria.	Analysis Evaluated
Safety- Continuation Phase	Comprises of all subjects in the DTG/ABC/3TC arm who receive at least one dose of study treatment after entering the Continuation Phase.	• Safety

Population	Definition/ Criteria.	Analysis Evaluated
ITT-E- Continuation Phase	Comprises of all subjects in the ITT-E population (as defined in Section 5) in the DTG/ABC/3TC arm who enter the Continuation Phase	• Study Population

12.13.3. Study Population

The study population summaries and data listings will be based on the ITT-E or ITT-E-Continuation Phase population, unless otherwise specified. Subject accountability summary will be produced for the overall study and separately for the Continuation Phase. Overview of the key planned study population endpoints:

- Study Populations
- Subject Accountability
- Concomitant and Antiretroviral Medications
- Protocol deviations

12.13.4. Safety Analysis

All safety displays will be based on the Safety population or Safety- Continuation Phase Population. The core adverse event displays for the final report have been identified based on the IDSL library required tables. For AE data (including COVID-19), unless stated otherwise, the summaries and listings will include only those AEs that occurred during Continuation Phase.
Summaries of AE required for the FDAAA and EudraCT will be generated in this reporting effort. Such summaries are identified in the Programming notes. These summaries will include participants from both Randomized and Continuation Phase.
Common AEs are those with >=3% (without rounding) incidence for any treatment.
One figure will be reported to present Maximum ALT vs. Maximum Total Bilirubin.
Overview of the key planned safety endpoints:

- Extent of Exposure
- Adverse Events
- Maximum Post-Baseline Emergent Clinical Chemistry/ Haematology Toxicities/ Hepatobiliary Laboratory Abnormality Criteria
- Liver Events Assessment
- Positive Suicidal indication Alerts based on eC-SSRS will be listed including data only in the Continuation Phase
- For subjects at Mexico sites and non-Mexico sites the following listings will be generated in this reporting effort. These listings will include data from both Randomized and Continuation Phase.
    - Listing of Non-Serious AEs of Subjects at Mexico sites
    - Listing of SAEs of Subjects at Mexico sites

- Listing of SAEs of Subjects at non-Mexico sites

12.13.5. Efficacy Analysis

The efficacy summaries and data listings will be based on the ITT-E population, unless otherwise specified. Subjects Randomized to the ATV+RTV+TDF/FTC arm completed the study after the Week 48 visit. Thus, the Snapshot algorithm that was used in the previous interim analyses would not be appropriate. Instead, HIV-1 RNA viral load will be summarized using observed data (i.e., subjects with missing data at a time point are excluded). The summaries and listings will be based on both Randomized and Continuation phase. Overview of the key planned efficacy endpoints:

- Absolute values in Plasma HIV-1 RNA and CD4+ Cell counts over time
- Proportion of Subjects with Plasma HIV-1 RNA < 50 c/ mL– observed data
- Proportion of subjects with Confirmed Virologic Withdrawal based on observed data.
- Change from Baseline in CD4+ cell count (cells/mm3) and Plasma HIV-1 RNA (log10 c/mL) by Visit
- Incidence of disease progression and HIV- associated conditions

12.13.6. Virology Analysis

The Virology displays will be based on ITT-E or Viral Genotypic and Viral Phenotypic populations. All virology summaries and Listings will include subjects who met Confirmed Virologic Withdrawal criteria during both Randomized and Continuation phase by separating the phases by page. Resistance testing will be performed on subjects at non-CVW time (ie, last on-treatment VL>400), and these subjects' viral data will be included only in the listing of resistance data for subjects at non-CVW time.

Prespecified lists of integrase substitutions have been modified since the previous interim analysis, hence an updated list of known INSTI mutations has been added in Table 8 and IAS-USA major resistance associated mutations (RAMs) to other classes (i.e., NRTI, NNRTI, PI) are listed in Table 9.

12.13.6.1. Genotype

Table 8 Known INSTI mutations associated with the development of resistance to RAL, EVG or DTG

Amino Acids in HIV Integrase for Analysis	H51Y, **T66A/I/K**, L74M, **E92Q/V**/G, Q95K, T97A, G118R, **F121Y**, E138A/K, G140A/C/S, **Y143C/H/R/K/S/G/A**, **P145S**, **Q146P**, **S147G**, **Q148**N/**H/K/R**, **V151**I/**L**/A, S153F/Y, **N155H**/S/T, E157Q, G163R/K, S230R, R263K, L68V/I*, L74I*, E138T*, G193E*

NOTES:

- Current listing includes INSTI mutations identified via the Stanford HIV Resistance database, or identified during in vitro passage of DTG, or as seen in a previous DTG studies in INSTI-experienced subjects (i.e. ING112574) and may be modified in case of additional substantive data availability.
- INSTI mutations in bold have the maximum score of 60 and are for any INSTI drug in the Stanford database v8.9 (http://hivdb.stanford.edu/DR/cgi-bin/rules_scores_hivdb.cgi?class=INSTI last updated on 25 OCT 2019 and accessed on 17 FEB 2020); the rest have a maximum score <60.
- The INSTI mutations listed are historically identified via the Stanford HIV Resistance database, and also include mutations identified during in vitro passage of DTG, or as seen in a previous DTG study in INSTI-experienced subjects (ING112574).

Table 9 Major resistance mutations to other classes (i.e., NRTI, NNRTI, PI) as defined by the International Antiviral Society-USA (IAS-USA).

Class	Mutations
NRTIs	M41L, K65R/E/N, D67N, 69 insert, K70E/R, L74V, Y115F, M184V/I, L210W, T215Y/F, K219Q/E; [A62V, V75I, F77L, F116Y, Q151M]
NNRTIs	L100I, K101E/P, K103N/S, V106A/M, V108I, E138A/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, I54V/M/L, Q58E, T74P, L76V, V82A/T/F/L/S, N83D, I84V, N88S, L90M

NOTES:

- Updated to "2019 Resistance Mutations Update Volume 27 Issue 3, July/August 2019
- The most up to date IAS-USA guidelines available at the time of DBF will be used in the analysis.
- Q151M Complex: Q151M usually occurs in combination with two or more of the following four accessory NRTI mutations A62V, V75I, F77L, and F116Y. However, if any one of these mutations occur alone, they shall be considered as major mutation for the NRTI class.

A mutation as treatment emergent in class XX, the subject must have received a drug YY in class XX as part of their study treatment, and the mutation must be associated with resistance to a drug in class XX and not present at baseline.

Stanford Genotypic Susceptibility Score (GSS)

- To establish genotypic susceptibility to ART treatment, a genotypic sensitivity score will be calculated.
- Genotypic sensitivity to each drug will be assessed using the HIVdb, the Integrated Genotypic Resistance Interpretation System [Liu, 2006].
- In the HIVdb system, each HIV-1 drug resistance mutation is assigned a drug penalty score. The penalty scores for each drug resistance mutation are available at
  NNRTI: https://hivdb.stanford.edu/dr-summary/mut-scores/NNRTI/
  NRTI: https://hivdb.stanford.edu/dr-summary/mut-scores/NRTI/
  PI: https://hivdb.stanford.edu/dr-summary/mut-scores/PI/
  INSTI: https://hivdb.stanford.edu/dr-summary/mut-scores/INSTI/. Scores for particular patterns of INSTIs are also available at https://hivdb.stanford.edu/dr-summary/pattern-scores/INSTI/

The drug resistance estimate is obtained by adding together the penalty scores from all mutations associated with resistance to that drug and then a numeric score (GSS) is applied for each drug as shown below. The sum scores are titrated to fall within the following ranges susceptible, potential low-level resistance, low-level resistance, intermediate resistance, and high-level resistance (see table below).

Resistance Estimate	S-GSS Score	Sensitivity
0 – 9	1	Susceptible
10 – 14	0.75	Potential low-level resistance
15 – 29	0.5	Low-level resistance
30 – 59	0.25	Intermediate resistance
≥60	0	High-level resistance

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

12.13.6.2. Phenotype

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

PSS with Full Sensitivity Only (PSSf)

Fold Change	Score	Interpretation
> clinical lower cutoff or biologic cutoff	0	resistance
≤ clinical lower cutoff or biologic cutoff	1	sensitive

PSS with Partial Sensitivity Included (PSSp)

Fold Change	Score	Interpretation
> clinical higher cutoff	0	resistance
≤ clinical higher cutoff and > clinical lower cutoff	0.5	partially sensitive
≤ clinical lower cutoff	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.

Clinical and Biological Cutoff Values for the PhenoSense HIV Drug Resistance Assay have changed since the previous interim analysis, hence for EoS phenotypic susceptibility will be categorised according to Fold Change as shown in Table 10 (based on Monogram PhenoSense assay).

Table 10 Clinical and Biological Cutoff Values for the PhenoSense HIV Drug Resistance Assay

Drug	Abbreviation	Class	PhenoSense Cutoff
Abacavir	ABC	NRTI	(4.5 – 6.5)[a]
Lamivudine	3TC	NRTI	3.5 [a]
Didanosine	ddI	NRTI	(1.3 – 2.2) [a]
Stavudine	d4T	NRTI	1.7 [a]
Zidovudine	AZT (ZDV)	NRTI	1.9
Emtricitabine	FTC	NRTI	3.5
Tenofovir	TDF	NRTI	(1.4 – 4) [a]
Delavirdine	DLV	NNRTI	6.2
Efavirenz	EFV	NNRTI	3
Nevirapine	NVP	NNRTI	4.5
Etravirine	ETR	NNRTI	(2.9-10) [a]
Rilpivirine	RPV	NNRTI	2.5
Fosamprenavir	FPV	PI	2 [a,c]
Fosamprenavir/r	FPV/r	PI	(4-11) [a]
Atazanavir	ATV	PI	2.2 [a,]
Atazanavir/r	ATV/r	PI	5.2 [a,c]
Indinavir/r	IDV/r	PI	10 [a]
Lopinavir/r	LPV/r	PI	(9 – 55) [a]
Nelfinavir	NFV	PI	3.6
Saquinavir	SQV	PI	1.7 [a,c]
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[b]
Raltegravir	RAL	INSTI	1.5
Elvitegravir	EVG	INSTI	2.5
Dolutegravir	DTG	INSTI	(4-13) [a]

a: clinical cutoff (lower cutoff – higher cutoff)
b: standard cut-off used by Monogram Inc. until clinical or biological cutoff have been determined
c: Only the boosted cutoff shall be used to compute the PhenoSense sensitivity for Atazanavir, Fosamprenavir and Saquinavir except stated otherwise.

Overview of the key planned virology endpoints:

- Genotypic and Phenotypic Accountability
- Major Mutations in NNRTI, NRTI and PI Classes and Pre-specified Mutations in INSTI from Baseline to Time of CVW
- Fold Change Summary of Fold Change to DTG at Baseline and Time of CVW

12.13.7. COVID-19 Analysis

This study started in 2013 and is being continued during the outbreak of the ongoing COVID -19 pandemic. The information regarding the number of subjects affected by COVID-19 and its symptoms will be reported according to GSK core standards. The visits impacted due to the pandemic outbreak will be reported. Protocol deviations or adverse events related to COVID-19 if any, will also be reported according to GSK core standards.

12.13.8. List of Data Displays for Final (End of Study)

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.1	All Subjects Screened	SA1	Summary of Study Populations	CS CORE; Only add the populations that will be used for EOS	EOS
1.7	ITT(E) - Continuation Phase	DV1a	Summary of Important Protocol Deviations by relationship to COVID-19 Pandemic-Continuation Phase	CS CORE	EOS

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.27	ITT(E) - Continuation Phase	Same as Week 48 Table 1.27	Summary of Subjects by Country and Investigator- Continuation Phase		EOS
1.28	ITT(E)	ES1	Summary of Subject Status and Subject Disposition by Relationship to COVID-19 Pandemic	FDAAA, EudraCT For overall, both phases Summarise by: i) Overall ii) Related to COVID-19, ii) Not related to COVID-19	EOS
1.29	ITT(E) - Continuation Phase	ES1	Summary of Subject Status and Subject Disposition by relationship to COVID-19 Pandemic- Continuation Phase	New Output; FDAAA, EudraCT Summarise by: i) Overall ii) Related to COVID-19, ii) Not related to COVID-19	EOS

Efficacy Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.7	ITT(E)	Same shell as ARIA Week 48 Table 2.7	Summary of Change from Baseline in Plasma HIV-1 RNA (log10 c/mL) by Visit		EOS
2.13	ITT(E)	Same shell as ARIA Week 48 Table 2.13	Proportion of Subjects Meeting Confirmed Virologic Withdrawal Criteria by Visit- Observed Case		EOS
2.15	ITT(E)	Same shell as ARIA Week 48 Table 2.15	Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) by Visit		EOS
2.16	ITT(E)	HIV1	Summary of Post-Baseline HIV-1 Associated Conditions Including Recurrences		EOS
2.17	ITT(E)	HIV1	Summary of Post-Baseline HIV-1 Associated Conditions Excluding Recurrences		EOS
2.18	ITT(E)	HIV2	Summary of Post-Baseline HIV-1 Disease Progressions		EOS
2.19	ITT(E)	gsk2619619/mid200336/final_01/table 2.1	Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Visit – Observed Case		EOS
2.20	ITT(E)	gsk2619619/mid200336/final_01/table 2.41	Summary of Absolute values in plasma HIV-1 RNA over time		EOS
2.21	ITT(E)	gsk2619619/mid200336/final_01/table 2.41	Summary of CD4+ cell counts over time		EOS

Efficacy Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.4	ITT(E)	Same shell as Gemini Figure 2.3	Individual Plasma HIV-1 RNA (log10 c/mL) and CD4+ Profiles by Visit for Subjects with at least One Suspected Virologic Withdrawal Visit		EOS

Safety Tables					
No	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.2	Safety	Same shell as Week 48 table 3.1	Summary of Extent of Exposure to Investigational Product	CS Core	EOS
3.52	Safety-Continuation Phase	Same shell as Week 48 table 3.1	Summary of Extent of Exposure to Investigational Product – Continuation Phase	New output	EOS
3.3	Safety-Continuation Phase	AE5	Summary of All Adverse Events by System Organ Class and Maximum Toxicity-Continuation Phase	CS Core	EOS
3.4	Safety-Continuation Phase	AE3	Summary of Common (>=3%) Adverse Events by Overall Frequency- Continuation Phase	CS Core	EOS
3.5	Safety-Continuation Phase	AE3	Summary of Common (>=3%) Grade 2-4 Adverse Events by Overall Frequency-Continuation Phase	CS Core	EOS
3.6	Safety-Continuation Phase	AE5	Summary of All Drug-Related Adverse Events by System Organ Class and Maximum Toxicity- Continuation Phase	CS Core	EOS
3.7	Safety-Continuation Phase	AE3	Summary of Common (>=3%) Drug-Related Grade 2-4 Adverse Events by Overall Frequency- Continuation Phase	CS Core	EOS
3.8	Safety-Continuation Phase	AE16	Summary of Serious Adverse Events by System Organ Class- Continuation Phase		EOS

3.9	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	CS Core New output. FDAAA, EudraCT	EOS
3.11	Safety-Continuation Phase	AE1	Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product – Continuation Phase	CS Core	EOS
3.13	Safety	AE3	Summary of Common (>=3%) Non-Serious Adverse Events	CS Core FDAAA	EOS
3.14	Safety	AE15	Summary of Common (>=3%) Non-Serious Adverse Events by System Organ Class and Preferred term (Number of Subjects and Occurrences)	CS Core EudraCT	EOS
3.29	Safety-Continuation Phase	Same shell as Week 48 Table 3.29	Summary of Maximum Post-Baseline Emergent Chemistry Toxicities –Continuation Phase	CS Core	EOS
3.30	Safety-Continuation Phase	Same shell as Week 48 Table 3.30	Summary of Maximum Post-Baseline Emergent Hematology Toxicities – Continuation Phase	CS Core	EOS
3.41	Safety-Continuation Phase	LIVER10	Summary of Subjects Meeting Hepatobiliary Laboratory Abnormality Criteria Post-Baseline Emergent-Continuation Phase		EOS
3.42	Safety-Continuation Phase	Same shell as ARIA Week 48	Subjects Meeting Hepatobiliary Abnormality Criteria - Post-Baseline Emergent-Continuation Phase		EOS

3.50	Safety-Continuation Phase	PAN1	Summary of COVID-19 Assessment for Subjects with COVID-19 Adverse Events-Continuation Phase	New Output	EOS
3.51	Safety-Continuation Phase	PAN3	Summary of COVID-19 Symptoms for Subjects with COVID-19 Adverse Events-Continuation Phase	New Output	EOS

Safety Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.3	Safety-Continuation Phase	LIVER9	Scatter Plot of Maximum ALT vs. Maximum Total Bilirubin-Continuation Phase-Continuation Phase	CS CORE	EOS
3.10	Safety	gsk1349572/ing111762/final_01/Figure 8.27	Plot of cumulative exposure to Investigational Product	New output;	EOS

Virology Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
7.9	Genotypic	PFG1	Summary of Major Mutations in NNRTI, NRTI and PI Classes and Pre-specified Mutations in INSTI Class at Baseline and time of CVW for Subjects Meeting CVW Criteria	New Output; For EoS both phases will be included.	EOS
7.10	Genotypic	gsk1349572/mid200304/primary_01/ Table 12.1	Summary of Subject Accountability: Genotypes Available	New Output; For EoS both phases will be included.	EOS
7.5	Phenotypic	Same shell as Week 48 Table 7.5	Summary of Phenotype at time of CVW by phenotypic cut-off	For EoS both phases will be included	EOS
7.7	Phenotypic	Same shell as Week 48 Table 7.7	Summary of Fold Change at Baseline and Time of CVW	For EoS both phases will be included.	EOS
7.11	Phenotypic	gsk1349572/mid200304/primary_01/ Table 12.6	Summary of Subject Accountability: Phenotypes Available	New Output; For EoS both phases will be included.	EOS

ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
4	ITT-E	ES2	Listing of Reasons for Study Withdrawal	CS CORE	EOS
6	ITT-E-Continuation Phase	DV2	Listing of Important Protocol Deviations - Continuation Phase	CS CORE	EOS
79	ITT-E-Continuation Phase	DV2	Listing of All Non-Important COVID-19 related Protocol Deviations-Continuation Phase	New Output	EOS
10	ITT-E	Same as Week 48 listing 10	Listing of Quantitative Plasma HIV-1 RNA Data		EOS
13	Safety	HIV_IP 5	Listing of Investigational Product Exposure Data	CS CORE	EOS
16	Safety-Continuation Phase	AE8	Listing of All Adverse Events-Continuation Phase	CS CORE	EOS
17	Safety-Continuation Phase	AE8	Listing of Fatal Adverse Events-Continuation Phase	CS CORE	EOS
18	Safety-Continuation Phase	AE8	Listing of Non-Fatal Serious Adverse Events-Continuation Phase	CS CORE	EOS
19	Safety-Continuation Phase	AE8	Listing of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product-Continuation Phase	CS CORE	EOS

ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
20	Safety-Continuation Phase	AE2	Listing of Relationship of Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text-Continuation Phase	CS CORE	EOS
22	Safety	LB5	Listing of Laboratory Data for Subjects with Grade 3 or 4 Post-Baseline Emergent Toxicities-Continuation Phase	CS CORE Use the shell of Listing 56 from gsk1349572/mid200304/primary_01/	EOS
25	Safety-Continuation Phase	PSRAE 1	Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Section 1- Section 2) - Continuation Phase		EOS
26	Safety-Continuation Phase	PSRAE 3	Listing of Possible Suicidality-Related Adverse Event Data: Possible Cause(s) (Section 3)- Continuation Phase		EOS
27	Safety-Continuation Phase	PSRAE 4	Listing of Possible Suicidality-Related Adverse Event Data (Section 4)- Continuation Phase		EOS
28	Safety-Continuation Phase	PSRAE 5	Listing of Possible Suicidality-Related Adverse Event Data (Section 5- Section 8)- Continuation Phase		EOS

Non-ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
29	All Subjects Screened	Same shell as ARIA Week 48 Listing 29	Listing of Study Populations		EOS
32	ITT-E	Same shell as ARIA Week 48 Listing 32	Listing of Visit Dates		EOS
40	ITT-E	Same shell as ARIA Week 48 Listing 40	Listing of Investigational Product Accountability		EOS
41	ITT-E-Continuation Phase	CM2	Listing of Concomitant Medications-Continuation Phase	CS CORE	EOS
45	ITT-E-Continuation Phase	CM2	Listing of Concomitant ART Medications-Continuation Phase		EOS
48	ITT-E	Same shell as ARIA Week 48 Listing 48	Listing of Subjects with Confirmed Virologic Withdrawal	Data in both Phases will be included	EOS
49	ITT-E	Same shell as ARIA Week 48 Listing 49	Listing of CD4+ Cell Count Data	Data in both Phases will be included	EOS
50	ITT-E	HIV4	Listing of HIV-1 Associated Conditions	Data in both Phases will be included	EOS
51	Safety	AE8	Listing of Non-Serious AEs of Subjects at Mexico sites	Mexican Safety Report requirement For EoS events in both phases will be included.	EOS

Non-ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
52	Safety	AE8	Listing of SAEs of Subjects at Mexico sites	Mexican Safety Report requirement For EoS events in both phases will be included.	EOS
53	Safety	AE8	Listing of SAEs of Subjects at non-Mexico sites	Mexican Safety Report requirement For EoS events in both phases will be included. Include the country in one column	EOS
65	Safety-Continuation Phase	LIVER5	Listing of Liver Event Results and Time of Event Relative to Treatment-Continuation Phase		EOS
69	Safety	MH2	Listing of Past and Current Liver Disease Medical Conditions		EOS
70	Safety-Continuation Phase	LB5	Listing of Laboratory Data from Liver Event Follow-Up-Continuation Phase		EOS
71	Safety-Continuation Phase	PREG1a	Listing of Subjects Who Became Pregnant During the Study-Continuation Phase		EOS

Non-ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
82	Safety-Continuation Phase	ECSSRS4	Listing of C-SSRS Suicidal Ideation and Behaviour Data-Continuation Phase	Add another column to show positive or negative.	EOS
83	Safety-Continuation Phase	PAN12	Listing of COVID-19 Assessments and Symptom Assessments-Continuation Phase	New Output	EOS
86	Safety-Continuation Phase	Same as Listing 13	Listing of Start and Stop dates in the Continuation Phase	New Output	EOS
76	ITT=E	Same shell as ARIA Week 48 Listing 76	Listing of All Genotypic Data	Both Randomized and Continuation Phase will be included in separate pages	EOS
78	ITT-E	Same shell as ARIA Week 48 Listing 78	Listing of All Phenotypic Data	Both Randomized and Continuation Phase will be included in separate pages	EOS
84	Genotypic and/or Phenotypic	/arenv/arprod/GSK1349572/ING111762/ final_01/Listing 37	Listing of Genotypic and Phenotypic Data for Subjects Meeting Confirmed Virologic Withdrawal Criteria	New Output; Both Randomized and Continuation Phase will be included in separate pages	EOS

Non-ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
85	ITT-E	/arenv/arprod/GSK1349572/ ING111762/ final_01/Listing 38.	Listing of Genotypic and Phenotypic Data for Subjects with On-Treatment Virology Results at Non-CVW Timepoints	New Output; Both Randomized and Continuation Phase will be included in separate pages	EOS

12.14. Appendix 14: List of Data Displays

12.14.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.n	1.1 to 1.n
Efficacy	2.1 to 2.n	2.1 to 2.n
Safety	3.1 to 3.n	3.1 to 3.n
Pharmacokinetic	4.1 to 4.n	4.1 to 4.n
Pharmacodynamic and / or Biomarker	5.1 to 5.n	5.1 to 5.n
Pharmacokinetic / Pharmacodynamic	6.1 to 6.n	6.1 to 6.n
Virology	7.1 to 7.n	NA
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	y to z	

12.14.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required an example mock-up displays provided in Appendix 15: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
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 / TST ID / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

12.14.3. Deliverable

Delivery	Description
WK48	Week 48 Statistical Analysis Complete
EOS	Final End of Study Statistical Analysis Complete

12.14.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.1.	All Subjects Screened	SA1	Summary of Study Populations	CS CORE;	WK48
1.2.	All Subjects Screened	ES6	Summary of Reasons for Screen Failure	CS CORE	WK48
1.3.	ITT(E)	EudraCT age	Summary of Age Categories	CS CORE	WK48
1.4.	ITT(E)	ES1	Summary of Subject Accountability: Randomized Phase Conclusion Record	FDAAA, EudraCT	WK48
1.5.	ITT(E)	ES1	Summary of Subject Accountability: Continuation Phase Conclusion Record	FDAAA, EudraCT	WK48
1.6.	ITT(E)	HIV_ES1	Summary of Subject Accountability: Withdrawals by Visit		WK48
1.7.	ITT(E) - Continuation Phase	DV1a	Summary of Important Protocol Deviations	CS CORE	WK48, EOS
1.8.	ITT(E)	SA2	Summary of Protocol Deviations Leading to Exclusion from the Per-Protocol Population	CS CORE	WK48
Demography					
1.9.	ITT(E)	DM1	Summary of Demographic Characteristics	CS CORE	WK48
1.10.	ITT(E)	DM5	Summary of Race and Racial Combinations	CS CORE	WK48
1.11.	ITT(E)	DM6	Summary of Race and Racial Combinations Details	CS CORE	WK48
1.12.	ITT(E)		Summary of Hepatitis Status at Entry		WK48
1.13.	ITT(E)	CDC1	Summary of CDC Classification of HIV Infection at Baseline		WK48

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.14.	ITT(E)	RF1	Summary of HIV Risk Factors		WK48
1.15.	ITT(E)		Summary of Baseline Cardiovascular Risk Assessments		WK48
1.16.	ITT(E)		Distribution of Quantitative Plasma HIV-1 RNA Results at Screening and Baseline		WK48
1.17.	ITT(E)		Distribution of CD4+ Cell Count (cells/mm^3) Results at Screening and Baseline		WK48
Medical Conditions, Concomitant Medications & ART					
1.18.	ITT(E)	MH1	Summary of Current Medical Conditions	CS CORE	WK48
1.19.	ITT(E)	MH1	Summary of Past Medical Conditions	CS CORE	WK48
1.20.	ITT(E)	MH4	Summary of Current Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, and Nervous System Conditions		WK48
1.21.	ITT(E)	MH4	Summary of Past Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, and Nervous System Conditions		WK48
1.22.	ITT(E)	CM1	Summary of Concomitant Medication by Ingredient ATC Level 1		WK48
1.23.	ITT(E)	CM8	Summary of Concomitant Medication Ingredient Combinations		WK48
1.24.	ITT(E)	CM1b	Summary of Concomitant Medication by Combination Term ATC Level 1		WK48
1.25.	ITT(E)		Summary of Lipid Modifying Agent Use at Baseline		WK48
1.26.	ITT(E)		Summary of Lipid Modifying Agent Use Starting Post-Baseline		WK48

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.27.	All Subjects Screened		Summary of Subjects by Country and Investigator		WK48

12.14.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Primary Efficacy Analyses					
2.1.	ITT(E)		Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 – Snapshot Analysis		WK48
2.2.	Per-Protocol		Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 – Snapshot Analysis		WK48
2.3.	ITT		Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 – Snapshot Analysis		WK48
2.4.	ITT(E)		Summary of Study Outcomes (<50 c/mL) at Week 48 – Snapshot Analysis		WK48
2.5.	ITT(E)		Treatment by Strata Tests of Homogeneity for Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 - Snapshot Analysis		WK48
Secondary Efficacy Analyses					
2.6.	ITT(E)		Summary of Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 by Subgroup - Snapshot Analysis		WK48
2.7.	ITT(E)		Summary of Change from Baseline in Plasma HIV-1 RNA (log10 c/mL) by Visit		WK48, EOS
2.8.	ITT(E)		Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Visit – Snapshot Analysis		WK48
2.9.	ITT(E)		Proportion of Subjects with Plasma HIV-1 RNA <400 c/mL by Visit – Snapshot Analysis		WK48

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.10.	ITT(E)		Summary of Study Outcomes (<400 c/mL) at Week 48 – Snapshot Analysis		WK48
2.11.	ITT(E)		Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Withdrawal at Week 48 *- Treatment Related Discontinuation = Failure*		WK48
2.12.	ITT(E)		Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Withdrawal at Week 48 *- Efficacy Related Discontinuation = Failure*		WK48
2.13.	ITT(E)	Same shell as ARIA Week 48	Proportion of Subjects Meeting Confirmed Virologic Withdrawal Criteria by Visit- Observed Case		WK48, EOS
2.14.	ITT(E)		Distribution of Quantitative Plasma HIV-1 RNA Results at Suspected and Confirmation of Confirmed Virologic Withdrawal		WK48
2.15.	ITT(E)	Same shell as ARIA Week 48	Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) by Visit		WK48, EOS
2.16.	ITT(E)	HIV1	Summary of Post-Baseline HIV-1 Associated Conditions Including Recurrences		WK48, EOS
2.17.	ITT(E)	HIV1	Summary of Post-Baseline HIV-1 Associated Conditions Excluding Recurrences		WK48, EOS
2.18.	ITT(E)	HIV2	Summary of Post-Baseline HIV-1 Disease Progressions		WK48, EOS
2.19.	ITT(E)	gsk2619619/ mid200336/ final_01/table 2.1	Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Visit – Observed Case		EOS

12.14.6. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Insert Endpoint Category					
2.1.	ITT(E)		Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL by Visit – Snapshot Analysis	Line plot	WK48
2.2.	ITT(E)	Same shell as Gemini Figure 2.3	Individual Plasma HIV-1 RNA (log10 c/mL) and CD4+ Profiles by Visit for Subjects with at least One Suspected Virologic Withdrawal Visit		WK48, EOS
2.3.	ITT(E)		Unadjusted Treatment Difference in Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL at Week 48 by Subgroup – Snapshot Analysis		WK48

12.14.7. Safety Figures

Safety : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Insert Endpoint Category					
3.1.	Safety	AE10	Plot of Common Adverse Events and Relative Risk	CS CORE	WK48
3.2.	Safety	LIVER9	Scatter Plot of Maximum vs. Baseline for ALT	CS CORE	WK48
3.3.	Safety	LIVER9	Scatter Plot of Maximum ALT vs. Maximum Total Bilirubin	CS CORE	WK48, EOS
3.4.	Safety		Line Plot of mean change from Baseline in Creatinine		WK48
3.5.	Safety		Bar Chart of Triglycerides (mmol/L) NCEP Categories at Week 48 vs. Baseline		WK48
3.6.	Safety		Bar Chart of Total Cholesterol (mmol/L) NCEP Categories at Week 48 vs. Baseline		WK48
3.7.	Safety		Bar Chart of HDL Cholesterol (mmol/L) NCEP Categories at Week 48 vs. Baseline		WK48
3.8.	Safety		Bar Chart of LDL Cholesterol (mmol/L) NCEP Categories at Week 48 vs. Baseline		WK48
3.9.	Safety		Bar Chart of Total Cholesterol/ HDL Ratio at Week 48 vs. Baseline		WK48

12.14.8. Health Outcomes Tables

Health Outcomes : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
SF-12					
6.1.	ITTE		Summary of SF-12 Individual Item Scores - LOCF		WK48
6.2.	ITTE		Summary of SF-12 Total score, MCS and PCS by Visit - LOCF	Results to go into summary stats come from a computer analysis progam	WK48
6.3.	ITTE		Summary of SF-12 Total score, MCS and PCS by Visit - Observed	Results to go into summary stats come from a computer analysis progam	WK48
6.4.	ITTE		Summary of Change from Baseline at Week 48 in SF-12 Total score, MCS and PCS - LOCF	Results to go into summary stats come from a computer analysis progam	WK48
6.5.	ITTE		Summary of Change from Baseline at Week 48 in SF-12 Total score, MCS and PCS - Observed	Results to go into summary stats come from a computer analysis progam	WK48
HIVTSQs					
6.6.	ITTE		Summary of HIVTSQs Individual Item Scores by Visit - LOCF		WK48
6.7.	ITTE		Summary of HIVTSQs Total Score by Visit - LOCF		WK48
6.8.	ITTE		Summary of HIVTSQs Total Score by Visit - Observed		WK48
6.9.	ITTE		Summary of HIVTSQs Lifestyle/ease Sub-score by visit - LOCF		WK48
6.10.	ITTE		Summary of HIVTSQs Lifestyle/ease Sub-score by visit - Observed		WK48
6.11.	ITTE		Summary of HIVTSQs General Satisfaction/Clinical Sub-score by visit - LOCF		WK48
6.12.	ITTE		Summary of HIVTSQs General Satisfaction/Clinical Sub-score by visit - Observed		WK48

12.14.9. Virology Tables

Virology : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Genotype					
7.1.	Genotypic		Summary of INI Mutations at time of CVW		WK48
7.2.	Genotypic		Summary of Treatment Emergent INI Mutations at time of CVW		WK48
7.3.	Genotypic		Summary of Major Mutations of NRTI, NNRTI and PI Classes at time of CVW		WK48
7.4.	Genotypic		Summary of Treatment Emergent Major Mutations of NRTI, NNRTI and PI Classes at time of CVW		WK48
Phenotype					
7.5.	Phenotypic		Summary of Phenotype at time of CVW by phenotypic cut-off	For EoS both phases will be included	WK48, EOS
7.6.	Phenotypic		Summary of Phenotype at time of CVW by Number of Drugs to Which Subject are Resistant		WK48
7.7.	Phenotypic		Summary of Fold Change at Baseline and Time of CVW	For EoS both phases will be included.	WK48, EOS
7.8.	Phenotypic		Summary of Change from Baseline in Fold Change at Time of CVW		WK48

12.14.10. Safety Tables

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Exposure					
3.1.	Safety		Summary of Extent of Exposure to Investigational Product – Randomised Phase	CS Core	WK48
3.2.	Safety		Summary of Extent of Exposure to Investigational Product – Randomisation and Continuation Phase	CS Core	WK48, EOS
Adverse Events					
3.3.	Safety	AE5	Summary of All Adverse Events by System Organ Class and Maximum Toxicity-Randomised Phase	CS Core	WK48, EOS
3.4.	Safety	AE3	Summary of Common (>=3%) Adverse Events by Overall Frequency-Randomised Phase	CS Core	WK48, EOS
3.5.	Safety	AE3	Summary of Common (>=3%) Grade 2-4 Adverse Events by Overall Frequency-Randomised Phase	CS Core	WK48, EOS
3.6.	Safety	AE5	Summary of All Drug-Related Adverse Events by System Organ Class and Maximum Toxicity-Randomised Phase	CS Core	WK48, EOS
3.7.	Safety	AE3	Summary of Common (>=3%) Drug-Related Grade 2-4 Adverse Events by Overall Frequency-Randomised Phase	CS Core	WK48, EOS
3.8.	Safety	AE1	Summary of Serious Adverse Events by System Organ Class – Randomised Phase	CS Core	WK48
3.9.	Safety	AE1	Summary of Serious Adverse Events by System Organ Class – Randomised and Continuation Phase	CS Core New output. FDAAA, EudraCT	WK48, EOS

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.10.	Safety	AE1	Summary of Drug-Related Serious Adverse Events by System Organ Class-Randomised Phase	CS Core Plain Language Summary (PLS) requirements	WK48
3.11.	Safety	AE1	Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product – Randomised Phase	CS Core	WK48
3.12.	Safety	AE1	Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product – Randomised and Continuation Phase	CS Core	WK48, EOS
3.13.	Safety	AE3	Summary of Common (>=3%) Non-Serious Adverse Events-Randomised and Continuation Phase	CS Core FDAAA	WK48, EOS
3.14.	Safety	EudraCT Non-serious AE	Summary of Subjects and Number of Occurrences of Common (>=3%) Non-Serious Adverse Events by System Organ Class-Randomised and Continuation Phase	CS Core EudraCT	WK48, EOS
3.15.	Safety	EudraCT SAE	Summary of Subjects and Number of occurrences of SAEs, Drug-related AEs, Fatal SAEs, and Drug-related SAEs-Randomised and Continuation Phase	CS Core EudraCT	WK48, EOS

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Laboratory					
3.16.	Safety	LB1	Summary of Chemistry Changes from Baseline by Visit	CS Core	WK48
3.17.	Safety	LB1	Summary of Lipids Percentage Changes from Baseline by Visit		WK48
3.18.	Safety	LB1	Summary of Hematology Changes From Baseline by Visit	CS Core	WK48
3.19.	Safety	LB1	Summary of Urine Concentrations Changes from Baseline by Visit	CS Core	WK48
3.20.	Safety		Summary of Maximum Post-Baseline in Urinalysis Dipstick Results		WK48
3.21.	Safety		Summary of Changes in Proteinuria Baseline Laboratory Result to Maximum Post-Baseline Laboratory Result - Randomised Phase	i.e., “shift table”	WK48
3.22.	Safety		Summary of Changes in NCEP Lipid Baseline Category to Maximum Post-Baseline Category - Triglycerides Randomised Phase		WK48
3.23.	Safety		Summary of Changes in NCEP Lipid Baseline Category to Maximum Post-Baseline Category – Total Cholesterol Randomised Phase		WK48
3.24.	Safety		Summary of Changes in NCEP Lipid Baseline Category to Maximum Post-Baseline Category – HDL Cholesterol Randomised Phase		WK48
3.25.	Safety		Summary of Changes in NCEP Lipid Baseline Category to Maximum Post-Baseline Category – LDL Cholesterol Randomised Phase		WK48

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.26.	Safety		Summary of TC/HDL ratio Changes from Baseline Randomised Phase		WK48
3.27.	Safety		Summary of Bone Markers Changes from Baseline Randomised Phase		WK48
3.28.	Safety		Summary of Maximum Post-Baseline Emergent Chemistry Toxicities – Randomised Phase	CS Core	WK48
3.29.	Safety		Summary of Maximum Post-Baseline Emergent Chemistry Toxicities – Randomised and Continuation Phase	CS Core	WK48, EOS
3.30.	Safety		Summary of Maximum Post-Baseline Emergent Hematology Toxicities – Randomised Phase	CS Core	WK48
3.31.	Safety		Summary of Maximum Post-Baseline Emergent Hematology Toxicities – Randomised and Continuation Phase	CS Core	WK48, EOS
3.32.	Safety		Statistical analysis of Change from Baseline in Triglycerides at Week 48 (Multiple imputed Dataset - MAR)		WK48
3.33.	Safety		Statistical analysis of Change from Baseline in Triglycerides at Week 48 - OC Dataset		WK48
3.34.	Safety		Statistical analysis of Change from Baseline in Triglycerides at Week 48 - Lipid LOCF Dataset		WK48
3.35.	Safety		Statistical analysis of Change from Baseline in Triglycerides at Week 48 - Repeated Measures Mixed Model Analysis		WK48
3.36.	Safety		Statistical analysis of Change from Baseline in TC/HDL Ratio at Week 48 (Multiple imputed Dataset - MAR)		WK48
3.37.	Safety		Statistical analysis of Change from Baseline in TC/HDL Ratio at Week 48 - Observed Case		WK48

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.38.	Safety		Statistical analysis of Change from Baseline in TC/HDL Ratio at Week 48 - Lipid LOCF		WK48
3.39.	Safety		Statistical analysis of Change from Baseline in TC/HDL Ratio at Week 48 - Repeated Measures Mixed Model Analysis		WK48

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Other					
3.40.	Safety	ABC_HSR1	Summary of the Incidence of Abacavir Hypersensitivity Reaction Classified as SAEs	Safety population, subset to those exposed to abacavir. Total column combines all treatment groups.	WK48
3.41.	Safety	OLIVER1	Summary of Subjects Meeting Hepatobiliary Abnormality Criteria at Any Post-Baseline Visit		WK48, EOS
3.42.	Safety		Subjects Meeting Hepatobiliary Abnormality Criteria - Post-Baseline Emergent		WK48, EOS
3.43.	Safety		Summary of Positive Suicidal indication Alerts based on eCSSRS by Visit		WK48
3.44.	Safety		Statistical Analysis of Bone Specific Alkaline Phosphatase (Ratio of Week 48 Result over Baseline)		WK48
3.45.	Safety		Statistical Analysis of Type I Collagen C-Telopeptides (Ratio of Week 48 Result over Baseline)		WK48
3.46.	Safety		Statistical Analysis of Osteocalcin (Ratio of Week 48 Result over Baseline)		WK48
3.47.	Safety		Statistical Analysis of Procollagen 1 N-Terminal Propeptide (Ratio of Week 48 Result over Baseline)		WK48
3.48.	Safety		Statistical Analysis of Vitamin D (Ratio of Week 48 Result over Baseline)		WK48
3.49.	Safety		Summary of All Adverse Events by System Organ Class - Randomised Phase		WK48

12.14.11. ICH Listings

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Study Population					
1.	Randomized	TA1	Listing of Randomized and Actual Strata and Treatment Assignment	CS CORE	WK48
2.	All Subjects Screened	ES7	Listing of Reasons for Screen Failure	CS CORE	WK48
3.	Randomized		Listing of Subjects Randomized But Not Treated	CS CORE (related to 'Listing for exclusion from any population)	WK48
4.	ITT-E	ES2	Listing of Reasons for Study Withdrawal	CS CORE	WK48, EOS
5.	ITT-E	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	CS CORE	WK48
6.	ITT-E		Listing of Important Protocol Deviations	CS CORE	WK48, EOS
7.	ITT-E		Listing of Protocol Deviations Leading to Exclusion from the Per-Protocol Population	CS CORE (add listing for exclusion of other populations?)	WK48
8.	ITT-E	DM2	Listing of Demographic Characteristics	CS CORE	WK48
9.	ITT-E	DM9	Listing of Race	CS CORE	WK48
Efficacy					
10.	ITT-E		Listing of Quantitative Plasma HIV-1 RNA Data		WK48, EOS
11.	ITT-E		Listing of Study Outcome (<50 c/mL) at Week 48 – Snapshot Analysis		WK48

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
12.	ITT-E		Listing of Study Outcome (<400 c/mL) at Week 48 – Snapshot Analysis		WK48
Safety					
13.	Safety	HIV_IP5	Listing of Investigational Product Exposure Data	CS CORE	WK48, EOS
14.	Safety		Listing of Investigational Product Exposure Data - Mexican Subjects		WK48
15.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events	CS CORE	WK48
16.	Safety	AE8	Listing of All Adverse Events	CS CORE	WK48, EOS
17.	Safety	AE8	Listing of Fatal Adverse Events	CS CORE	WK48, EOS
18.	Safety	AE8	Listing of Non-Fatal Serious Adverse Events	CS CORE	WK48, EOS
19.	Safety	AE8	Listing of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product	CS CORE	WK48, EOS
20.	Safety-Continuation Phase	AE2	Listing of Relationship of Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	CS CORE For EoS only report events in the Continuation Phase; Add "-Continuation Phase to the title"	WK48, EOS

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
21.	Safety	SAE Reasons	Listing of Reasons for Considering as a Serious Adverse Event	CS CORE FDA	WK48
22.	Safety	LB5	Listing of Clinical Chemistry Laboratory Data for Subjects with Laboratory Abnormalities of Potential Clinical Concern	CS CORE	WK48, EOS
23.	Safety	LB5	Listing of Hematology Laboratory Data for Subjects with Laboratory Abnormalities of Potential Clinical Concern	CS CORE	WK48
24.	Safety	UR2a	Listing of Urinalysis Data for Subjects with Abnormalities of Potential Clinical Concern	CS CORE	WK48
25.	Safety	PSRAE1	Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Section 1- Section 2)		WK48, EOS
26.	Safety	PSRAE3	Listing of Possible Suicidality-Related Adverse Event Data: Possible Cause(s) (Section 3)		WK48, EOS
27.	Safety	PSRAE4	Listing of Possible Suicidality-Related Adverse Event Data (Section 4)		WK48, EOS
28.	Safety	PSRAE5	Listing of Possible Suicidality-Related Adverse Event Data (Section 5- Section 8)		WK48, EOS

12.14.12. Non-ICH Listings

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Study Population					
29.	All Subjects Screened		Listing of Study Populations		WK48, EOS

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
30.	All Subjects Screened		Listing of Subject Recruitment by Country and Site Number		WK48
31.	All Subjects Screened		Listing of Rescreened Subjects		WK48
32.	ITT-E		Listing of Visit Dates		WK48, EOS
33.	ITT-E		Listing of Hepatitis Test Results		WK48
34.	ITT-E	CDC3	Listing of CDC Classification of HIV Infection at Baseline		WK48
35.	ITT-E	RF2	Listing of HIV Risk Factors		WK48
36.	ITT-E	MH2	Listing of Current and Past Medical Conditions at Baseline		WK48
37.	ITT-E		Listing of Current and Past Medical Conditions at Baseline - Mexican subjects only		WK48
38.	ITT-E		Listing of Baseline Cardiovascular Risk Assessment Data		WK48
39.	ITT-E		Listing of History of Cardiac Therapeutic Procedures		WK48
40.	ITT-E		Listing of Investigational Product Accountability		WK48, EOS
41.	ITT-E	CM2	Listing of Concomitant Medications	CS CORE	WK48, EOS
42.	ITT-E		Listing of Concomitant Medications - Mexican subjects only		WK48
43.	ITT-E	CM6	Listing of Relationship Between ATC Level 1, Ingredient and Verbatim Text		WK48
44.	ITT-E	CM2	Listing of Prior ART Medications		WK48
45.	ITT-E	CM2	Listing of Concomitant ART Medications		WK48, EOS
46.	ITT-E		Listing of Concomitant ART Medications - Mexican subjects only		WK48

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
47.	ITT-E	CM6	Listing of Relationship Between ATC Level 4, Ingredient and Verbatim Text		WK48
Efficacy					
48.	ITT-E	Same shell as ARIA Week 48	Listing of Subjects with Confirmed Virologic Withdrawal		WK48, EOS
49.	ITT-E	Same shell as ARIA Week 48	Listing of CD4+ Cell Count Data		WK48, EOS
50.	ITT-E	HIV4	Listing of HIV-1 Associated Conditions		WK48, EOS
Safety					
51.	Safety	AE8	Listing of Non-Serious AEs of Subjects at Mexico sites	Mexican Safety Report requirement For EoS events in both phases will be included.	WK48, EOS
52.	Safety	AE8	Listing of SAEs of Subjects at Mexico sites	Mexican Safety Report requirement	WK48, EOS
53.	Safety	AE8	Listing of SAEs of Subjects at non-Mexico sites	Mexican Safety Report requirement	WK48, EOS
54.	Safety	AE8	Listing of Pre-treatment Adverse Events		WK48

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
55.	Safety		Listing of Cardiovascular Events		WK48
56.	Safety	VS4	Listing of Vital Signs		WK48
57.	Safety	ABC_HSR _EXPO2	Listing of Abacavir Hypersensitivity Reaction Record - Exposure to Abacavir		WK48
58.	Safety	ABC_HSR _DRUG2	Listing of Abacavir Hypersensitivity Reaction Record - Subject History of Drug Allergies		WK48
59.	Safety	ABC_HSR COND2	Listing of Abacavir Hypersensitivity Reaction Record - Subject and Family Conditions		WK48
60.	Safety	ABC_HSR _RASH2	Listing of Abacavir Hypersensitivity Reaction Record - Skin Rash Details		WK48
61.	Safety	ABC_HSR _SYMP4	Listing of Abacavir Hypersensitivity Reaction Record - Symptoms		WK48
62.	Safety	VS4	Listing of Abacavir Hypersensitivity Reaction Record - Vital Signs		WK48
63.	Safety	ABC_HSR _SYMP6	Listing of Abacavir Hypersensitivity Reaction Record - Individual Symptoms and Diagnostic Category Assignments (Excluding Other Symptoms)		WK48
64.	Safety	ABC_HSR _SYMP7	Listing of Abacavir Hypersensitivity Reaction Record - Individual Symptoms and Diagnostic Category Assignments (Other Symptoms)		WK48
65.	Safety	LIVER5	Listing of Liver Event Results and Time of Event Relative to Treatment		WK48, EOS
66.	Safety	LIVER6	Listing of Liver Event Information for RUCAM Score		WK48
67.	Safety	LIVER7	Listing of Liver Biopsy Details		WK48
68.	Safety	LIVER8	Listing of Liver Imaging Details		WK48

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
69.	Safety	MH2	Listing of Past and Current Liver Disease Medical Conditions		WK48, EOS
70.	Safety	LB5	Listing of Laboratory Data from Liver Event Follow-Up		WK48, EOS
71.	Safety	PREG1a	Listing of Subjects Who Became Pregnant During the Study		WK48, EOS
72.	Safety	ECSSRS4	Columbia Suicidality		WK48, EOS
81.	Safety		Listing of Post Baseline Maximum ALT and Maximum Bilirubin - Randomised Phase		WK48
82.	Safety		Listing of Positive Suicidal Alerts Based on eCSSRS		WK48
Health Outcomes					
75.	ITT-E		Listing of HIVTSQs		WK48
Pharmacokinetic Analysis					
80.	Safety		Listing of Pharmacokinetic Concentration Data		WK48
Virology					
76.	Genotypic	ARIA Week 48 Listing 76	Listing of All Genotypic Data	Both Randomized and Continuation Phase will be included in separate pages	WK48, EOS
77.	Genotypic		Listing of Treatment Emergent Genotypic Mutations		WK48
78.	Phenotypic	ARIA Week 48 Listing 78	Listing of All Phenotypic Data	Both Randomized and Continuation Phase will be included in separate pages	WK48, EOS

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
79.	Phenotypic		Listing of Replication Capacity		WK48

12.15. Appendix 15: Example Mock Shells for Data Displays

Data display specifications will be uploaded as separate document.