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

Title	:	Reporting and Analysis Plan for 201585 (ATLAS) A Phase III, randomized, multicenter, parallel-group, non-inferiority, open-label study evaluating the efficacy, safety, and tolerability of switching to long-acting cabotegravir plus long-acting rilpivirine from current INI- NNRTI-, or PI-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed
Compound Number	:	GSK1265744
Effective Date	:	20-JUN-2018

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 201585
- This RAP is also intended to describe the statistical analysis considerations (including derivation of key endpoints, baseline definitions, analysis visit windows, and data handling conventions) for IDMC interim analyses; details of the planned displays provided in the IDMC charter.
- This RAP will be provided to the study team members to convey the content of the Week 48/96/end of study: Statistical Analysis Complete (SAC) deliverable.

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for protocol

GlaxoSmithKline Protocol Number	Date	Version
2015N252007_00	2016-MAY-26	Original
2015N252007_01	2016-SEP-16	Amendment No. 1
The purpose of this amendment is to support country-specific requirements for South Korea including an update to inclusion criteria age for local regulatory requirements and the addition of study investigational product labels within Appendix 8.		
2015N252007_02	2016-NOV-02	Amendment No. 2
The purpose of this amendment is to support country-specific requirements for Sweden based on local regulatory requirements and to provide additional protocol details and clarifications requested by the MPA.		
2015N252007_03	2016-DEC-13	Amendment No. 3
The reasons for this amendment were to: update medical monitor/SAE contact information; provide additional clarity for assessments to be conducted during the Extension Phase; add text to instruct contact of the Medical Monitor upon the occurrence of rash during the CAB + RPV oral lead-in period; specify a secondary lipid objective and endpoint within the study objectives; provide clarity around dosing at the Day 1 visit; allow serum pregnancy testing instead of urine testing in the event that urine testing is not available; provide clarification that cabotegravir and rilpivirine exposure may persist for more than one year following IM injections, emphasize that participants should continue to use HAART for at least one year following the last CAB + RPV injection, and that female participants of childbearing potential must continue to use adequate contraception for at least one year after the last CAB + RPV injection; expand the allowance of short treatment courses of topical, inhaled, or intranasal glucocorticoids to 21 days or less; add additional guidance for the definition of a change in ART regimen for inclusion/exclusion criteria; provide additional guidance on when to contact the Medical Monitor upon a serofast RPR result for screening syphilis test; clarify language within exclusion criteria #9; added text regarding the treatment assignment randomization schedule; remove a requirement to record within the eCRF how frequently IP was taken on average and the requirement to record any treatment delays or dose reductions of IP; add text to indicate that drugs known to cause Torsade des Pointes (TdP) should be used with caution with rilpivirine; remove limits on the duration for use of topical imiquimod; add clarity around reflexive testing for HBV DNA for participants with positive anti HBc and negative HBsAg and negative anti-HBs results; add temperature collection as part of vital signs to the Time and Events table; add requirement that all sites should have a plan in place for managing possible risks for suicide related events; clarify text regarding PK sample		

window collection; clarify text for patient reported outcome endpoints and timings for completion of questionnaires relative to other clinical assessments and procedures, add clarification for prohibited medication information; remove information in the Appendix requiring collection of pregnancy information for female partners of male study participants; incorporate updates from country-specific amendments No 1, and No 2. into a global protocol amendment; add text that additional details of the injection device used by sites for IM administration including, but not limited to functional performance, may also be collected within the eCRF; clarify that commercially availability of CAB LA + RPV LA includes availability through local public/government health sectors; add allowance that in exceptional circumstances, local labs can be reviewed and approved by the Medical Monitor for consideration of participant eligibility; add information that Screening HLA-B*5701 result is not required to inform eligibility status; add other minor corrections and edits to protocol text.		
2015N252007_04	2017-NOV-02	Amendment No. 4
The reason for amendment 4 is to acknowledge the potential rollover of eligible 201585 (ATLAS) study participants following the Week 52 visit and completion of time point for the primary analysis to the 207966 (ATLAS-2M) study examining the efficacy, safety and tolerability of CAB LA + RPV LA administered every 4 weeks (Q4W) compared to CAB LA + RPV LA administered every 8 weeks (Q8W). Specifications for the procedural rollover of 201585 participants are included within amendment #4. Due to the planned transition of eligible participants to ATLAS-2M following the time point completing Week 48 primary analysis, the snapshot virologic response at Week 96 and in the Extension Phase for ATLAS is no longer valid and has been replaced with the proportion of participants with plasma HIV-1 RNA < 50 c/mL over time including Week 96. Exploratory analyses evaluating the effect of patient characteristics on virologic and immunologic responses in the treatment arms are also limited to a Week 48 analysis. The reporting timeline of pregnancy event and follow-up pregnancy form has been updated from 2 weeks to 24 hrs of identification of a pregnancy event, and within 24 hrs of investigator awareness of pregnancy outcome, respectively. Updated references for the cabotegravir and rilpivirine investigator brochures have been added.		

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the protocol / protocol amendment #4 [(Dated: 02/NOV/2017)].
OR
Changes from the originally planned statistical analysis specified in the protocol are outlined in Table 1.

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
No change	No change	

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

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
To demonstrate the non-inferior antiviral activity of switching to intramuscular CAB LA + RPV LA every 4 weeks (monthly) compared to continuation of current first line antiretroviral regimen over 48 weeks in HIV-1 infected antiretroviral therapy (ART)-experienced participants	• Proportion of participants with a 'virologic failure' endpoint as per Food and Drug Administration (FDA) Snapshot algorithm at Week 48 (Intent-to-Treat Exposed [ITT-E] population).
Secondary Objectives	**Secondary Endpoints**
To demonstrate the antiviral and immunologic activity of switching to intramuscular CAB LA + RPV LA every 4 weeks (monthly) compared to continuation of current ART	• Proportion of participants with Plasma HIV-1 RNA <50 copies/mL (c/mL) at Week 48 using the FDA Snapshot algorithm (Missing, Switch or Discontinuation = Failure, Intent-to-Treat Exposed [ITT-E] population). • Proportion of participants with plasma HIV-1 RNA <200 c/mL at Week 48 using the Snapshot algorithm (ITT-E population) • Proportion of participants with confirmed virologic failure (two consecutive plasma HIV-1 RNA levels ≥200 c/mL after prior suppression to <200 c/mL) through Week 48 • Absolute values and change from Baseline in plasma HIV-1 RNA (log_{10} c/mL) at Week 48. • Absolute values and change from Baseline in CD4+ lymphocyte count at Week 48 • Incidence of disease progression (HIV-associated conditions, acquired immunodeficiency syndrome [AIDS] and death over 48 Weeks
To evaluate the safety and tolerability of switching to CAB LA + RPV LA every 4 weeks (monthly) compared to continuation of current ART	• Incidence and severity of adverse events (AEs) and laboratory abnormalities over time including Week 48 • Proportion of participants who discontinue treatment due to AEs over time including Week 48 • Absolute values and changes in laboratory parameters over time including Week 48
To evaluate the effects of CAB LA + RPV LA every 4 weeks on fasting lipids over time compared to continuation of	• Change from Baseline in fasting lipids over time including Week 48 and Week 96.

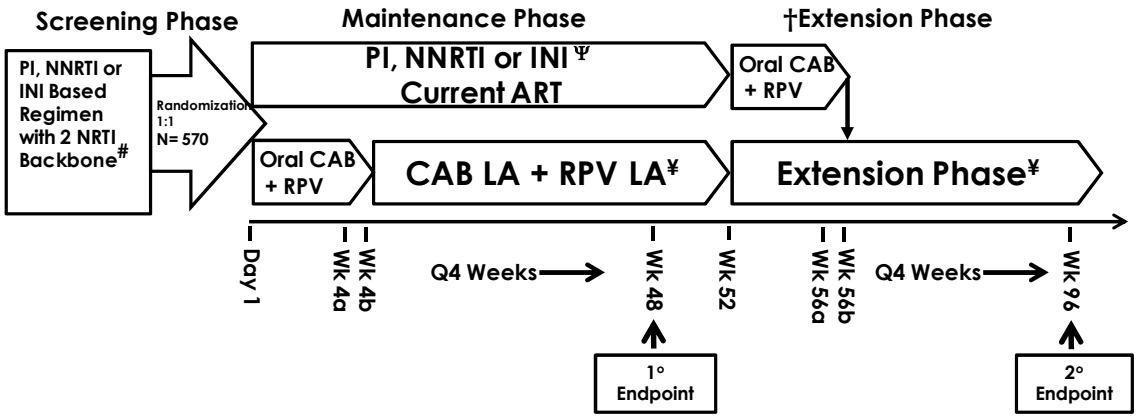
Objectives	Endpoints
current ART over time.	
To assess viral resistance in participants experiencing confirmed virologic failure (CVF)	• Incidence of treatment emergent genotypic and phenotypic resistance to CAB, RPV and other on-study ART through Week 48
To assess the impact of Baseline third agent treatment class (INI, NNRTI, or PI) on efficacy, safety, tolerability, and viral resistance of CAB LA + RPV LA compared to continuation of current ART	<u>By Baseline third agent treatment class:</u> • Proportion of participants with a 'virologic failure' endpoint as per FDA Snapshot algorithm at Week 48 (Intent-to-Treat Exposed [ITT-E] population). • Proportion of participants with Plasma HIV-1 RNA <50 c/mL at Week 48 using the FDA Snapshot algorithm (Intent-to-Treat Exposed [ITT-E] population) • Incidence and severity of select AEs and laboratory abnormalities over time including Week 48 • Proportion of participants who discontinue treatment due to AEs over time including Week 48 • Absolute values and changes in select laboratory parameters over time including Week 48 • Incidence of observed genotypic and phenotypic resistance to current antiretroviral regimen and to CAB or RPV for participants meeting confirmed virologic failure (CVF)
To characterize CAB and RPV concentrations and population pharmacokinetics and identify important determinants of variability.	• Plasma PK parameters for CAB LA and RPV LA (when evaluable, $C_{trough,}$ concentrations post dose [~Cmax], and area under the curve [AUC]) • Demographic parameters including, but not limited to, age, sex, race, body weight, body mass index, and relevant laboratory parameters will be evaluated as potential predictors of inter- and intra-participant variability for pharmacokinetic parameters
To evaluate the antiviral and immunologic effects, safety, tolerability, and viral resistance of CAB LA + RPV LA for participants during the Extension Phase • For participants randomized to CAB LA+ RPV LA at Day 1 • For participants electing to	• Proportion of participants with plasma HIV-1 RNA < 50 c/mL over time including Week 96 (observed case) • Proportion of participants with confirmed virologic failure (two consecutive plasma HIV-1 RNA levels ≥200 c/mL after prior suppression to <200 c/mL)

Objectives	Endpoints
transition to CAB LA + RPV LA in the Extension Phase	through Week 96 • Absolute values and change from Baseline in plasma HIV-1 RNA over time including Week 96 • Absolute values and changes from Baseline in CD4+ cell counts over time including Week 96 • Incidence of disease progression (HIV-associated conditions, acquired immunodeficiency syndrome [AIDS] and death) • Incidence and severity of AEs and laboratory abnormalities over time including Week 96 • Proportion of participants who discontinue treatment due to AEs over time including Week 96 • Absolute values and changes in laboratory parameters over time including Week 96 • Incidence of treatment emergent genotypic and phenotypic resistance to CAB, RPV, and other on study ART through Week 96
To assess the acceptance of pain and injection site reactions following injections	• Change from Week 5 in Dimension scores (“Bother of ISRs”, “Leg movement”, “Sleep”, and “ Injection Acceptance”) and individual item scores assessing pain during injection, anxiety before and after injection, willingness to be injected in the future and overall satisfaction with mode of administration over time using the Perception of iNjection questionnaire (PIN) • Proportion of participants considering pain and local reactions following injection to be extremely or very acceptable based on the acceptability score over time using the Perception of iNjection questionnaire (PIN)
To assess degree of health-related quality of life (HRQoL)	• Change from Baseline in HR QoL using the HIV/AIDS-targeted quality of life questionnaire (HAT QoL) short form at Week 24, Week 48, Week 96 (or Withdrawal).
To assess the health status	• Change from Baseline in health status at Week 24, Week 48, and Week 96 (or Withdrawal) using the 12-item Short Form Survey (SF-12). .
To assess treatment satisfaction of CAB LA + RPV LA compared to	• Change from baseline in total “treatment satisfaction” score, and individual items scores of the HIVTSQs at

Objectives	Endpoints
continuation of current ART	Weeks 4b, 24, 44, 96 (or Withdrawal) • Change in treatment satisfaction over time using the HIVTSQc at Week 48 (or Withdrawal)
To assess treatment acceptance	• Change from Baseline in treatment acceptance at Week 8, Week 24, Week 48, Week 96 (or Withdrawal) using the "General acceptance" dimension of the Chronic Treatment Acceptance (ACCEPT) questionnaire
To assess tolerability of injections	• Change from Week 4b in tolerability of injection at Week 5, Week 40, Week 41, and Week 96 using the Numeric Rating Scale (NRS) within the CAB + RPV LA arm.
Exploratory Objectives	**Exploratory Endpoints**
To explore the effect of patient characteristics (e.g., demographic factors, Baseline CD4+) on the virologic and immunologic responses to CAB LA+ RPV LA compared to continuation of current ART	• Proportion of participants by patient subgroup(s) (e.g., by age, gender, BMI, race, HIV-1 subtype, Baseline CD4+) with Virologic Failure over time including Week 48 using the Snapshot algorithm for the ITT-E population • Proportion of participants by patient subgroup(s) (e.g., by age, gender, body mass index (BMI), race, HIV-1 subtype, Baseline CD4+) with plasma HIV-1 RNA <50 c/mL over time including Week 48 using the Snapshot algorithm for the ITT-E population • Change from Baseline in CD4+ cell counts by subgroups at Week 48
To explore relationship(s) between plasma concentrations of CAB and RPV and pharmacodynamic endpoints.	• Relationship between plasma PK concentrations and virologic, immunologic responses, and/or occurrence of adverse events [AEs] over time may be explored.
To evaluate renal and bone biomarkers in participants treated with CAB LA + RPV LA compared to continuation of current ART	• Absolute value and change from Baseline in renal (in urine and blood), and bone (in blood) over time
To assess preference for CAB LA+ RPV LA compared to oral ARV using a single dichotomous preference question.	• For patients randomized to the "CAB LA + RPV LA" arm, preference for CAB LA + RPV LA compared to oral ARV regimen, at Week 48 • For patients randomized to the "Current ART" arm who switched to the injectable treatment, preference for CAB LA + RPV LA compared to current ART regimen at Week 96 (end of extension phase-secondary analysis)
To assess reason for switching using a single question.	• The reasons for willingness to switch ART at baseline for both treatment arms and for patients randomized to the "Current ART" arm at Week 52.

2.3. Study Design

Overview of Study Design and Key Features



N=570, randomized 1:1 to each arm and stratified by baseline 3rd Agent class and sex at birth.
# Must be on uninterrupted current regimen (either the initial or second cART regimen) for at least 6 months prior to Screening.Documented evidence of at least two plasma HIV-1 RNA measurements <50 c/mL in the 12 months prior to Screening: one within the 6 to 12 month window, and one within 6 months prior to Screening. No history of virologic failure. No evidence of viral resistance based on the presence of any resistance-associated major INI, or NNRTI mutation (except K103N) from prior genotype assay results. No current or prior history of etravirine use.
ΨINI based regimen excludes abacavir/dolutegravir/lamivudine (TRIUMEQ), and INI therapy will be capped at approximately 40% of study enrolment for current ART
†Optional Extension Phase to CAB LA + RPV LA at Wk 52 for participants randomized to current ART
¥Participants who withdraw from IM arm must go into 52 week long term follow up phase

Design Features	• Phase III, randomized, open-label, active-controlled, multicenter, parallel-group, non-inferiority study designed to assess the antiviral activity and safety of a two-drug regimen of CAB LA + RPV LA compared with maintenance of current ART • The ATLAS study comprises a Screening Phase (up to 35 days), a Maintenance Phase (Day 1 to Week 52), and the randomized portion of the study will continue with an Extension Phase up to at least 96 weeks Additionally, any participant who receives at least a single dose of CAB LA and/or RPV LA and discontinues the CAB LA + RPV LA regimen will enter the Long-term Follow-up Phase and will initiate highly active antiretroviral therapy (HAART) for at least 52 weeks after the last dose of CAB LA and/or RPV LA
Dosing	• Maintenance Phase: 1:1 randomization to continue current ART or be switched to the CAB LA + RPV LA regimen through 52 weeks • Extension Phase: CAB LA + RPV LA
Treatment Assignment	• N =570 randomized at start of Maintenance Phase • At Week 52, participants randomized to continue on current ART will have the option to either continue study participation by switching to CAB LA + RPV LA in the Extension Phase, or to complete their study participation at

Overview of Study Design and Key Features	
	Week 52. • GSK RandAll NG used to generate randomization schedules • Stratified Randomization by baseline third agent class (PI, INI, or NNRTI) and sex at birth.
Interim Analysis	• 50% of subjects completing Week 24 • Continuous time monitoring of confirmed virologic failure (CVF) (both in the NNRTI strata and overall) • The main analysis will be conducted to evaluate the primary objective of the protocol at Week 48. • Further data cuts and analyses may be conducted as necessary in order to support regulatory submissions and publications.

2.4. Statistical Hypotheses / Statistical Analyses

The study is designed to demonstrate that the antiviral effect of switching to CAB LA + RPV LA (CAB) is non-inferior to continuation of current first line antiretroviral regimen (current ART) at Week 48 in HIV-1 infected ART-experienced participants. Non-inferiority in the proportion of participants with HIV-1 RNA ≥ 50 copies/mL at Week 48 (per FDA's snapshot algorithm) can be concluded if the upper bound of a two-sided 95% confidence interval for the difference in the proportion of subjects with HIV-1 RNA ≥ 50 copies/mL between the two treatment arms (CAB – current ART) is less than 6%.

If f_{la} is the rate of subjects with HIV-1 RNA ≥ 50 c/mL on CAB LA + RPV LA and f_c is the rate of subjects with HIV-1 RNA ≥ 50 c/mL (per FDA snapshot algorithm) for the Current ART arm then the hypotheses can be written as follows:

H0: $f_{la} - f_c \geq 6\%$ H1: $f_{la} - f_c < 6\%$

In the pooled analysis of the two studies, as described in the clinical summary analysis plan, a 4% non-inferiority margin will be used.

3. PLANNED ANALYSES

At least two analyses will be conducted to evaluate primary and secondary objectives of the protocol, one after all subjects have completed their visit at Week 48 and one after Week 96. Further data cuts and analyses may be conducted as necessary after Week 96 in order to support regulatory submissions and publications. The Week 48 analysis will be primary, at which primary and secondary comparisons between arms will be performed. There will be no comparison between treatment arms at Week 96 analyses. An IDMC analysis will be conducted when about 50% subjects have completed Week 24, and a final End-of-Study (EOS) analysis will be conducted when all subjects have completed the study.

3.1. Interim Analyses

An Independent Data Monitoring Committee (IDMC) will be instituted to ensure external objective medical and/or statistical review of efficacy and safety in order to protect the ethical interests and well-being of subjects and to protect the scientific validity of this study and study 201584.

An IDMC will evaluate accumulating efficacy, tolerability / safety, and PK of CAB LA + RPV LA at predetermined times during the study. An interim futility analysis will be performed with the intent of having approximately 50% of participants reaching Week 24 and providing sufficient lead time to allow the IDMC to review the data prior to any participants reaching the Week 48 visit. A futility rule based on Bayesian posterior predictive probability approach will be applied to assess the probability that CAB LA + RPV LA injectable regimen would demonstrate non-inferiority to the continued the Current ART arm given the partial data set. The Sponsor will remain blinded to this analysis.

In addition, the IDMC may also monitor the incidence of participants meeting confirmed virologic failure criteria until all subjects complete Week 24 to ensure that participants are not being sub-optimally treated in the CAB + RPV LA arm.

Full details of the analyses, estimated timing and the decision criteria that will be used to determine regimen performance will be pre-specified in the IDMC Charter.

3.2. Final Analyses

The primary analysis will be conducted to evaluate the primary objective of the protocol at Week 48. These analyses will be performed after the completion of the following sequential steps:

1. All subjects have completed Week 48 and had a re-test if necessary.
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. Randomization codes have been distributed according to Ramos NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Subjects Screened Population	• 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
All Participants Randomized Population	• All randomized participants	• Secondary population for some analyses
Intent-to-Treat Exposed Population (ITT-E)	• All randomized participants who receive at least one dose of IP during the Maintenance Phase of the study (on or after Day 1 visit). • Participants will be analysed according to the randomized treatment regardless of what treatment was actually received.	• Study Population • Efficacy
Per-Protocol (PP)	• Consist of all participants in the ITT-E Population with the exception of those with important protocol deviations leading to exclusion from PP population. Important protocol deviations that would exclude subjects from the PP population are defined in Section 4.1 (Protocol Deviations) and Appendix 1 (Protocol Deviation Management and Definition for Per-Protocol Population).	• Efficacy (Sensitivity Analysis)
Safety population	• All randomized participants who receive at least one dose of IP during the Maintenance Phase of the study (on or after Day 1 visit). • Participants will be assessed according to actual treatment received	• Safety
Extension Switch Population (ESP)	• All randomized subjects from Current ART arm who receive at least one dose of CAB and/or RPV during the Extension Phase of the study.	• Safety and efficacy
The Safety Long-Term Follow-up Population (LTFU)	• All subjects receiving at least one dose of CAB LA and/or RPV LA who have discontinued the CAB LA+ RPV LA regimen and have a least one Long-Term Follow-up phase clinic visit.	• Safety
PK Population	• All participants who receive CAB and / or RPV and undergo PK sampling during the study, and provide CAB and /or RPV plasma concentration data.	• PK
Confirmed Virologic Failure	Comprised of all subjects in the ITT-E population who met Confirmed Virologic Failure (CVF)	• Genotypic • Phenotypic

Population	Definition / Criteria	Analyses Evaluated
(CVF) Population	criteria. *CVF is defined as: Rebound as indicated by two consecutive plasma HIV-1 RNA levels ≥200 c/mL after prior suppression to <200 c/mL	• IDMC CVF Analysis
Futility Analysis Population at Week 24	• Comprised of all subjects in the ITT-E population and who started study treatment at least 169 days prior to the IDMC cut-off date (in order to account for subjects who withdrew early but would have achieved Week 24)	• IDMC Futility Analysis

NOTES:

- Please refer to Appendix 13: List of Data Displays which details the population to be used for each display being generated.

4.1. 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 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.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG Randomization System		Data Displays for Reporting	
Code	Description	Description	Order in TLF
A	CAB LA + RPV LA	Q4W IM	1
B	Current ART	Current ART	2

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

Q4W IM vs Current ART

5.2. Baseline Definitions at Maintenance

Baseline is referred to Baseline at Maintenance, unless otherwise specified. For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-treatment (see Table 9) assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline.

Electrocardiograms (ECGs) are to be performed in triplicate on Day 1 visit. The baseline value for an ECG parameter will be the mean of the last pre-treatment set of assessments from the same date, so long as at least one of the triplicate assessments is available.

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

5.3. Multicentre Studies

Data will be summarized for all centres combined. Country will be treated as an exploratory subgroup for analyses of the primary efficacy endpoint as described in Section 7.1.5.1. Some countries will be combined for exploratory subgroup analyses with consideration due to the number of participants enrolled. These include (but are not limited to) those identified below

Region	Countries
Latin America	Argentina + Mexico

5.4. Examination of Covariates, Other Strata and Subgroups

5.4.1. Covariates and Other Strata

The list of covariates and other strata may be used in descriptive summaries and statistical analyses, some of which may also be used for subgroup analyses. Additional covariates and other strata of clinical interest may also be considered.

Category	Details
Strata	Randomization Strata: For the proportion of participants with plasma HIV-RNA greater than or equal to 50 copies/mL per FDA Snapshot algorithm at Week 48 (primary endpoint), a stratified analysis with Cochran-Mantel Haenszel weights will be used to adjust the primary treatment comparison for the randomization strata corresponding to sex at birth and third agent class at entry). A similar approach will be used to adjust the analysis of the proportion of participants with HIV-1 RNA <50 c/mL (per the FDA's Snapshot algorithm) at Week 48 (key secondary endpoint). See Section 7.1.5.1 for additional details on the statistical analysis methodology.
Other Subgroups/Covariates	See details in Section 5.4.2

5.4.2. Examination of Subgroups/Covariates

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

- If the percentage of subjects is small within a particular subgroup, then the subgroup categories may be redefined 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.
- For subgroup analysis, per European Medicines Agency Guideline on the investigation of subgroups in confirmatory clinical trials (EMA, 2013), factors defining a subgroup population may be put in three categories:
  EMA Subgroup Category 1: Factors with strong reason to expect a heterogeneous response to treatment. In this case separate trials should usually be planned. There are no factors falling into this category in this study.

  EMA Subgroup Category 2: Factors with at least some biological plausibility or external evidence such that a heterogeneous response might be hypothesized. In this study, stratified randomisation strata, key demographic factors, Baseline CD4, CDC stage will be fall into this category. For these factors, subgroup analyses will be performed but likely underpowered so that a formal proof of efficacy will not be available individually in all subgroups. If consistent findings across multiple

comparisons were observed then these analyses would still be suggestive of a generalizable finding from the overall population.
EMA Subgroup Guideline Category 3: Factor with good argumentation why homogeneity of response to treatment is plausible. The impact of factors falling into this category will be explored.

- Additional covariates of clinical interest may also be considered.

Category	Covariates and / or Subgroups
EMA Subgroup Category 2:	
Stratified Randomisation Strata	• Baseline third agent class (PI, INI, NNRTI) • Sex at birth (Male, Female) For analysis purposes, randomization strata will be derived using eCRF data, even if this differs from the strata captured in RAMOS NG. 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: o <35; 35-<50; ≥50 (for statistical modelling on efficacy analysis of PK/PD and health outcome, the first two groups will be consolidated, i.e. <50, ≥50) For the Table of summary of demographic characteristics only, the following age group should also be presented: <=18, 19-64, >=65 (FDAAA requirement) 18-64, 65-84, >=85 (EMA requirement) • Race: o White; Non-White o Black/ African American; Non- Black/ African American • Country o Argentina o Mexico o Australia o Canada o France o Germany o Italy

Category	Covariates and / or Subgroups
	○ Korea, Republic of ○ Russian Federation ○ South Africa ○ Spain ○ Sweden ○ United States • Baseline viral load: ○ <50; ○ ≥ 50 copies/mL. • Baseline CD4+ cell count: ○ <200; ○ 200 to <350; ○ 350 to <500; ○ ≥ 500 cells/mm^3. • Derived Baseline Centres for Disease Control and Prevention (CDC) category: ○ Stage I ○ Stage II ○ Stage III
EMA Subgroup Category 3:	
Additional subgroup/covariates for PK/PD efficacy analysis	• Last CAB/RPV Trough PK concentration (i.e. pre-dose PK concentration wk48) • Week-8 CAB/RPV Trough PK concentration (i.e. pre-dose PK concentration at nominal visit of Week 8) Dichotomized into two subgroups: ≤ first Quartile vs > first quartile, ≤ Median vs > Median, The Concentration will be treated as continuous variable in logistic regression modelling analysis (i.e. the concentration data will be log2 transformed in this analysis so that, for assessing the effect, one unit increase of the point estimate of $\log_2$ PK concentration is equivalent to 'doubling the concentration' in the original value). If pre-dose PK concentration at wk48 is missing, then last pre-dose PK concentration prior to WK48 will be used • BMI (<30, ≥ 30 kg/m2) at Baseline

Category	Covariates and / or Subgroups
	• Length of Injection Needle (<2, ≥2 inch) For PK/PD efficacy analysis, length of injection needle at Week 4B will be used.
Additional subgroup/covariates for PK/PD safety analysis	• Last CAB/RPV trough PK concentration For the plot of Maximum Change from Baseline(CFB) in ALT/Total Bilirubin versus Last Trough CAB/RPV PK Concentrations, Last CAB/RPV Trough PK concentration is the most recent trough PK concentration prior or equal to the date of Lab assessment with maximum CFB, at Maintenance phase For the Plot of Maximum Toxicity Grades of Most Frequently Reported AEs versus Last Trough CAB/RPV PK Concentrations, Last CAB/RPV Trough PK concentration is the most recent trough PK concentration prior or equal to the onset date of the most frequently reported AE with maximum toxicity grade, at Maintenance phase. If a subject has no AE most commonly reported, then the last trough value at Maintenance phase will be used for the plot
Additional subgroup for Bone Marker analysis	• BMI (kg/m2) at Baseline o <30 o ≥ 30 • Smoking status: o never, o current, o former • taking Tenofovir (TDF) at Baseline o Yes o No
Additional subgroup for ISR	• Length of Injection Needle (<2, ≥2 inch) for CAB and RPV, separately. For the summary of maximum graded ISR event by length of needle and causal agent (CAB vs RPV) will be determined based on the reported side of the ISR and the side of the previous injection administration up to and including the maximum graded ISR onset date. If we are unable to determine the needle length/causal agent in those events where both drugs are given on one side and/or their needle lengths are different, then the attribution to a needle length/causal agent will remain unknown and the ISR will be excluded from this

Category	Covariates and / or Subgroups
	summary. If there is no ISR of interest reported during maintenance phase for a subject, the needle length of last injection during Maintenance phase will be used in this summary.

5.5. Multiple Comparisons and Multiplicity

5.5.1. Primary Comparison of Interest

The primary analysis will be based on the ITT-E population. The primary comparison will be made at a one-sided 2.5% level of significance. Treatment with Q4W IM will be declared non-inferior to Current ART if the upper end of a two-sided 95% confidence interval for the difference between the two groups (Q4W IM– Current ART) in the proportion of participants with HIV-RNA ≥50 c/mL at Week 48 (defined by the US FDA snapshot algorithm) lies below 6%.

The primary comparison of interest is the comparison between Q4W IM and Current ART for the primary endpoint in the ITT-E population. This analysis will be adjusted for by the stratification factor applied at randomization.

If the primary analysis (Section 5.5.1) shows non-inferiority then a superiority hypothesis will be tested at the two-sided 5% level of significance. Superiority favoring CAB LA + RPV LA will be declared if the upper end of the confidence interval is below 0% for the ITT-E population analysis. If superiority is declared, the p-value for superiority will also be calculated.

5.5.2. Secondary comparison

- If the primary comparison on interest (Section 5.5.1) using the ITT-E population demonstrates non-inferiority of Q4W compared to Current ART then the following key secondary comparisons using the ITT-E population will be tested: Treatment with Q4W IM will be declared non-inferior to Current ART with respect to the proportion of participants with HIV-1 RNA < 50 copies/mL at Week 48 (defined by the US FDA snapshot algorithm) if the lower end of a two-sided 95% confidence interval for the difference between in rates (Q4W IM– Current ART) lies above -10% using the ITT-E population
- Superiority of Q4W IM compared to Current ART respect to change from baseline in HIVTSQs, at Week 44 using a two-sided 5% level of significance
- Changes in the PIN acceptance score within the CAB LA + RPV LA arm at Week 48 from Week 5 using a two-sided 5% level of significance

There are no planned adjustments for multiple comparisons or multiplicity.

For the primary endpoint treatment comparison at Week 48, no multiple comparison adjustment is necessary for testing non-inferiority followed by superiority (conditional on achieving a significant test for non-inferiority) since testing follows a pre-specified

sequence of hypothesis such that if the first hypothesis tested is not significant, all subsequent tests will not be performed. This fixed sequence procedure controls the type I error rate at the nominal level.

In addition to the primary and the key secondary comparisons, the comparisons between two treatment arms for ACCEPT (general acceptance score), SF-12 (health status), and HATQoL (Life satisfaction) at timepoints through Week 48 will also be performed as supportive analyses.

Lastly, for the IDMC interim analyses, since the statistical stopping guidelines will not result in early stopping for positive efficacy findings, these interim treatment comparisons will not inflate the Type I error rate for the primary treatment comparison.

5.6. Other Considerations for Data Analyses and Data Handling Conventions

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

Section	Component
Section 13.2	Appendix 2: Schedule of Activities
Section 13.3	Appendix 3: Assessment Windows
Section 13.4	Appendix 4: Study Phases and Treatment State
Section 13.5	Appendix 5: Data Display Standards & Handling Conventions
Section 13.6	Appendix 6: Derived and Transformed Data
Section 13.7	Appendix 7: Reporting Standards for Missing Data
Section 13.8	Appendix 8: Values of Potential Clinical Importance
Section 13.9	Appendix 9: Population Pharmacokinetic (PopPK) Analyses
Section 13.10	Appendix 10: Pharmacokinetic / Pharmacodynamic Analyses
Section 13.11	Appendix 11: Snapshot Algorithm Details
Section 13.14	Appendix 14: IDMC
Section 13.15	Appendix 15: Variables Defined for Time to Event Analysis
Section 13.16	Appendix 16: Example Mock Shells for Data Displays

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the Intent-to-Treat Exposed population, unless otherwise specified.

Study population analyses including analyses of subject's disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, and exposure and treatment compliance will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 13: List of Data Displays.

Table 2 provides an overview of the planned study population analyses, with full details of data displays being presented in Section 13.13: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated	
	Table	Listing
Randomisation		
Randomisation [1]		Y[2]
Subject Disposition		
Study Populations [3]	Y	Y[4]
Study Recruitment [3]	Y	Y
Reasons for Screening Failures [3]	Y	Y
History of Rescreened Subjects [3]		Y
Age categories	Y	
Subject Disposition	Y[5][6]	
Reasons for Withdrawal by Visit	Y[5][6]	Y
IP discontinuation	Y	Y
Important Protocol Deviations	Y	Y
Deviations leading to exclusion from PP	Y	Y
Inclusion and Exclusion Criteria Deviations	Y	Y
Demography and Baseline		
Demographics Characteristics [7]	Y	Y
Race & Racial Combinations [8]	Y	Y
Hepatitis Status	Y	Y
CDC Classification of HIV infection (2014)	Y	Y
Cardiovascular Risk Assessments at Baseline	Y	Y
Distribution of CD4+ Cell Counts	Y	
History of Cardiac Therapeutic Procedures		Y

Display Type	Data Displays Generated	
	Table	Listing
Medical Conditions, Concomitant Medications & Antiretroviral Therapy		
Medical Conditions (Current/Past) [9]	Y	Y
Medical Conditions: Sub-conditions (Current/Past) [9, 10]	Y	
Concomitant Medications (non-ART)	Y[11]	Y[12]
Antiretroviral Therapy stopped Prior to Screening [13]	Y	Y[14]
Antiretroviral Therapy Taken during Screening	Y	Y[15]
Antiretroviral Therapy Taken Prior to & during Screening for Subjects Failing ART Eligibility Criteria		Y
Concomitant Antiretroviral Therapy at Maintenance Phase	Y	Y[15]
Baseline third agent class (Strata) [16]	Y	Y
Lipid Modifying agents (Baseline and Post-Baseline)	Y	
Substance use	Y	Y
Other		
Study Treatment Accountability[17]		Y

NOTES:

- T = Tables, L = Listings, Y = Display Generated,

1. All Participants Randomized population
2. One listing of subjects randomized but not treated, and one listing of planned and actual treatment strata.
3. All Subjects screened population.
4. Listing will be based on all subjects screened population
5. 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.
6. Analysis of subject disposition will be performed for each study phase separately, as well as for overall study conclusion.
7. Age and ethnicity collected at Screening; weight and height collected at Day 1
8. 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.
9. Medical conditions will be coded using the Medical Dictionary for Regulatory Activities (MedDRA).
10. Sub conditions are Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, and Nervous System Conditions
11. 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 labeled 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).)
12. One listing for concomitant non-ART medications and one listing showing the relationship between verbatim text, ingredient and ATC Level 1.
13. Include medications that started and stopped prior to 6 months before screening
14. One listing for Prior ART stopped prior to Screening and one listing showing the relationship between verbatim text, ingredient, combination and ATC Level 4 for all ART.
15. Separate Listing of for ART taking during Screening and taken concomitant ARTs
16. Based on the actual third agent class derived from the eCRF CONART data collection of what the subjects actually took, regardless of the strata they were randomized into.
17. Dispensation information (dates and number of tablets dispensed and returned).

7. EFFICACY ANALYSES

7.1. Primary Efficacy Analyses

7.1.1. Endpoint / Variables

Where applicable, describe the method for combining measurements to create composite variables. Flexibility to include this information in Proportion of participants with plasma HIV-RNA greater than or equal to 50 copies/mL as per Food and Drug Administration (FDA) Snapshot algorithm at Week 48 (Intent-to-Treat Exposed [ITT-E] population); see Section 13.11 for additional details. Appendix 6: Derived and Transformed Data.

7.1.2. Summary Measure

Difference in the proportion of participants with HIV-RNA ≥50 c/mL at Week 48 (defined by the US FDA snapshot algorithm) between each treatment group (Q4W IM – Current ART).

7.1.3. Population of Interest

The primary efficacy analyses will be based on the Intent-To-Treat Exposed population, unless otherwise specified.

7.1.4. Strategy for Intercurrent (Post-Randomization) Events

As defined by the Snapshot algorithm, HIV-RNA ≥ 50 copies/mL is determined by the last available HIV-1 RNA measurement while the participant is on treatment within the analysis visit window of interest.

Participants without evaluable HIV-RNA data for the visit of interest and who discontinue treatment for reasons not related to adverse event while having HIV-1 RNA ≥ 50 copies/mL at time of discontinuation or who change study treatment not permitted per protocol before the analysis window are classified as having HIV-RNA ≥ 50 copies/mL.

7.1.5. Statistical Analyses / Methods

Table 3 provides an overview of the planned efficacy analyses. Details of the planned displays are provided in Appendix 13: List of Data Displays and will be based on GSK data standards and statistical principles.

Table 3 Overview of Planned Primary Efficacy Analyses

Endpoints	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Proportion of Subjects with 'HIV-1 ≥ 50 c/mL' at Week 48 – Snapshot							
Primary analysis of comparison between the two groups (CAB – current ART) in 'HIV-1 RNA≥50' rates at Week 48	Y[1]			Y[1,2]	Y[4]		Y[2]
Treatment Heterogeneity across randomization strata	Y						
By Subgroup [3] (Exploratory analysis to support primary analysis)				Y[5]	Y[4]		

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) and 'Per-Protocol' (sensitivity) populations.
2. Study outcomes (i.e., response below 50 c/mL, 'HIV-1 RNA≥50' or reason for no data in the window) based on the snapshot algorithm.
3. Randomisation Strata, demographic and Baseline Characteristics (refer to Section 5.4).
4. Plot of the difference in proportion of subjects ≥50 c/mL (Snapshot algorithm) and its 95% confidence intervals for 'overall' (on the top of the figure) and by subgroup at Week 48.
5. Study outcomes based on the Snapshot algorithm by subgroup at Week 48 will also be produced.

7.1.5.1. Statistical Methodology Specification

Primary Statistical Analyses

Endpoint

- Proportion of Participants with Plasma HIV-1 ≥ 50 c/mL at Week 48 using the Snapshot algorithm for the ITT-E population. 'HIV-1 RNA≥50' are based on the Snapshot algorithm includes subjects who had plasma HIV-1 RNA ≥ 50 c/mL at Week 48, who discontinued for lack of efficacy, who discontinued for other reasons while not <50 c/mL, or who changed ART).

Snapshot Dataset

- Virologic outcome ('HIV-RNA <50' or '≥50 copies/mL') per Snapshot algorithm is determined by the last available on-treatment HIV-1 RNA measurement within the analysis visit window of interest (please refer to analysis window defined in Table 11). In addition, subjects who discontinue for reasons not related to adverse event with on-treatment HIV-1 RNA result at the time of discontinuation ≥ 50 copies/mL or who change study treatment not permitted per protocol during maintenance phase before the analysis visit are classified as 'HIV-RNA ≥ 50 copies/mL'.
- Full details of the Snapshot algorithm are provided in Section 13.11.

Model Specification

- The primary efficacy endpoint will be analysed using a stratified analysis with Cochran-Mantel-Haenszel (CMH) weights, adjusting Baseline third agent class (PI, INI, or NNRTI) and sex at birth
- 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 Baseline analysis strata resulting from the cross classification of both stratification factors:
    - Baseline third agent class PI AND Male sex at birth
    - Baseline third agent class PI AND Female sex at birth
    - Baseline third agent class INI AND Male sex at birth
    - Baseline third agent class INI AND Female sex at birth
    - Baseline third agent class NNRTI AND Male sex at birth
    - Baseline third agent class NNRTI AND Female sex at birth
- If n_k is the number of CAB LA + RPV LA treated subjects, m_k is the number of the control arm 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

Primary Statistical Analyses

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

are CMH weights and $\hat{d}_k$ are estimates of the differences in proportions between the two treatment arms, f_{Q8W}-f_{Q4W}, for the *kth* stratum.

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

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

where the variance estimator [Sato, 1989] is consistent in both sparse data and large strata and is given below

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

where

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

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

with x_k and y_k corresponding to the number of participants with Plasma HIV-1 ≥ 50 c/mL at Week 48 per FDA Snapshot for CAB LA + RPV LA and Current ART, respectively, for the *kth* stratum.

Model Results Presentation

- Adjusted CMH estimate of the difference in the proportion of subjects with 'HIV-1 RNA≥50'between each treatment group (CAB LA + RPV LA – Current ART) and corresponding 95% confidence interval.
- Non-inferiority will be concluded if the upper bound of the two-sided 95% confidence interval (CI) for the CMH adjusted difference in proportion of subjects with 'HIV-1 RNA≥50' in the CAB LA + RPV LA group minus proportion of subjects with 'HIV-1 RNA≥50' in the Current ART group is less than 6%.
- If the analysis shows non-inferiority then a superiority hypothesis will be tested at the two-sided 5% level of significance. Superiority favoring CAB LA + RPV LA will be declared if the upper end of the confidence interval is below 0% for the ITT-E population analysis. If superiority is declared, the p-value for superiority will also be calculated.

Primary Statistical Analyses

Subgroup 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. Exploration of Subgroup
   - An analysis for subgroups listed in Section 5.4.2 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 subgroups. These results will also be presented graphically.
3. Summary of study outcomes (i.e., response below 50 c/mL, 'HIV-1 RNA≥50'or reason for no data in the window) by subgroup will be produced.
4. Note: These subgroup analyses will be exploratory and likely underpowered so that interpretation may therefore focus on point estimates as well as the upper 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.

Sensitivity and Supportive Analyses

1. Per-protocol population analysis:
   To assess the impact of important 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.

7.2. Secondary Efficacy Analyses

7.2.1. Endpoint / Variables

Proportion of participants with plasma HIV-1 RNA <50 c/mL (c/mL) at Week 48 using the FDA Snapshot algorithm (Intent-to-Treat Exposed [ITT-E] population).

7.2.2. Summary Measure

Difference in the proportion of participants with HIV-RNA < 50 c/mL at Week 48 (defined by the US FDA snapshot algorithm) between each treatment group (Q4W IM – Current ART).

7.2.3. Population of Interest

The secondary efficacy analyses will be based on the Intent-to-Treat Exposed population, unless otherwise specified.

7.2.4. Strategy for Intercurrent (Post-Randomization) Events

Participants with last available HIV-1 RNA measurement less than 50 copies/mL while the participant is on treatment within the analysis visit window of interest are classified as responders.

Participants without evaluable HIV-RNA data for the visit of interest or who change treatment not permitted per protocol before the analysis window are considered non-responders.

7.2.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 13: List of Data Displays and will be based on GSK data standards and statistical principles.

Table 4 provides an overview of the planned efficacy analyses. Details of the planned displays are provided in Appendix 13: List of Data Displays and will be based on GSK data standards and statistical principles.

Table 4 Overview of Planned Secondary Efficacy Analyses

Endpoints	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Proportion of Participants with Plasma HIV-1 < 50 c/mL at Week 48 – Snapshot[1]							
Key secondary analysis	Y[2]			Y[2, 3]	Y		Y[3]
Treatment Heterogeneity across randomization strata	Y						
Proportion of Participants without efficacy-related discontinuation (ERDF) or treatment-related discontinuation (TRDF) failure (refer to Section 13.6.4)							
Kaplan-Meier estimate				Y			
Proportion of Subjects with Plasma HIV-1 RNA ≥50 copies/mL over time through Week 48– Snapshot							
by Visit				Y	Y[4]		
by Visit and Subgroup[5]				Y	Y		

Endpoints	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL over time through Week 48– Snapshot							
by Visit				Y	Y[6]		
by Visit and Subgroup [5]				Y	Y[7]		
Proportion of Subjects with Plasma HIV-1 RNA <200 copies/mL over time through Week 48– Snapshot (also for ≥200 copies/mL)							
by Visit				Y[8]	Y[9]		
Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL at Week 48 by delay in IP injection [10] - Snapshot (exploratory analysis)							
by Delay in IP injection				Y			Y
Proportion of Subjects with Plasma HIV-1 RNA <2 copies/mL (exploratory analysis)							
by Visit - Observed Case Analysis				Y			Y

1. This analysis will be performed using the similar approach as described for the primary analysis in Section 7.1.5.1
2. Generated using the 'Intent-to-Treat Exposed' (primary) and 'Per-Protocol' (sensitivity) populations.
3. Study outcomes (i.e., response below 50 c/mL, 'HIV-1 RNA≥50'or reason for no data in the window) based on the snapshot algorithm.
4. Line plots, with 95% confidence intervals(CIs), for the proportion of subjects HIV-1 RNA ≥50c/mL for overall and by treatment group at each visit. The 95% CIs will be calculated using Exact (Clopper-Pearson) confidence interval if the proportion is 0%. Otherwise, they are derived using the normal approximation.
5. Randomisation strata, Baseline and demographic factors (refer to Section.5.4)
6. Line plots, with 95% confidence intervals, for the proportion of subjects <50c/mL by treatment group at each visit.
7. Plot of the difference in proportion of subjects <50 c/mL and its 95% confidence intervals (Snapshot algorithm) by subgroup for Week 48 only.
8. Study outcomes (i.e., HIV-1 RNA< 200 c/mL, HIV-1 RNA≥200c/mL, or reason for no data in the window) based on the snapshot algorithm by subgroup for Week 48 will also be produced.
9. Line plots, with 95% confidence intervals, for the proportion of subjects <200c/mL and ≥200 c/mL by treatment group at each visit.
10. Delay in IP injection (days) is defined in Section 13.6.4

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 [1]				Y		Y[2]	Y[3]							
Detected vs Non-detected by Visit [5]				Y			Y[6]							
Confirmed Virologic Failure (CVF)														
CVF by Visit				Y			Y							
HIV-1 RNA at time of suspected and confirmed Virologic Failure				Y										
CD4+ , CD8+ Cell Counts Over Time														
CD4+ Observed				Y							Y			Y
CD8+ observed				Y							Y			Y
CD4+/CD8+ ratio observed				Y										
Post-baseline HIV-1 Conditions and Disease Progression														
HIV Conditions including/excluding Recurrences as recorded in eCRF				Y			Y							
HIV Disease Progressions [4]				Y										

NOTES:

- T = Table, F = Figures, L = Listings, 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. Using observed case (OC) data which contains the data that is available at a particular time point, with no imputation for missing values.
2. Individual plasma HIV-1 RNA only for subjects who are in the category of 'viral load ≥50 c/mL' at Week 48 per Snapshot algorithm or who are CVF subjects. The figures will display all HIV-1 RNA values observed.
3. Include the interpretation of whether the virus is detected or not ('Detected' or 'Not detected') by the assay.
4. HIV disease progressions (Section 13.6.4)
5. See Section 13.6.4 for a definition of "Target Detected" and "Target Non-detected".
6. Included in the Observed HIV-1 RNA listing

7.2.5.1. Statistical Methodology Specification

Key Secondary Statistical Analyses
Endpoint
Proportion of participants with plasma HIV-1 RNA <50 c/mL at Week 48 using the FDA Snapshot algorithm (Intent-to-Treat Exposed [ITT-E] population)
Snapshot Dataset
• As described in Section 7.1.5.1 and Section 13.11
Model Specification
• As specified in Section 7.1.5.1 but with HIV-1 RNA <50 c/mL (Snapshot Success) replacing Plasma HIV-1 ≥ 50 c/mL (Snapshot 'HIV-1 RNA≥50')
Model Results Presentation
• Adjusted CMH estimate of the difference in the proportion of participants with plasma HIV-1 RNA <50 c/mL at Week 48 between each treatment group (Q4W – Current ART) and corresponding 95% confidence interval. • Non-inferiority will be concluded if the lower bound of the two-sided 95% confidence interval for the CMH adjusted treatment difference (Q4W – Current ART) is greater than -10%.
Subgroup Analyses
• Treatment Heterogeneity across randomization strata: o As specified in Section 7.1.5.1 but with Snapshot Success (HIV-1 RNA <50 c/mL) replacing Snapshot HIV-1 RNA ≥ 50 c/mL.
Sensitivity and Supportive Analyses
1. Per-protocol population analysis: To assess the impact of important 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.

8. SAFETY ANALYSES

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

For the week 48 primary analysis and IDMC, outputs will be presented for the Maintenance Phase unless otherwise specified.

For the Week 48 primary analysis, a set of separate outputs will also be presented for the oral lead-in period at Maintenance phase, including summary of adverse events, SAE, AE leading to withdrawal, post-baseline emergent chemistry/haematology abnormality, subjects with hepatobiliary abnormality criteria et al.

For the Week 96 secondary analysis, outputs will be presented for the Maintenance + Extension phases for subjects randomized to receive CAB +RPV LA, and will be presented for the Extension phase only for Extension Switch Population (ESP). Adverse events by System Organ Class and Maximum Toxicity for Long-term Follow-up Phase will also be summarized.

8.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 13: List of Data Displays.

8.2. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Haematology laboratory tests, Urinalysis, and liver function tests will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 13: List of Data Displays.

8.3. Other Safety Analyses

The analyses of non-laboratory safety test results including ECGs and vital signs will be based on GSK Core Data Standards, unless otherwise specified. The details of the planned displays are presented in Appendix 13: List of Data Displays.

ECG Values of Potential Clinical Interest are defined as a QTc of > 450ms or a change from baseline in QTc of > 30ms per IDSL standard.

8.4. Planned Safety Analysis

Table 5 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 13: 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[1]	Y			Y[2]								
adherence to Q4W dosing [1]	Y			L								
Injection Needle												
Length and Gauge	Y			Y								
Adverse Events[3]												
All AEs by SOC	Y											
All AEs by SOC and Toxicity[3]	Y			Y[4]								
Common AEs by freq [5]	Y	Y[6]										
Common Grade 2-5 AEs [5] by freq	Y											
All Drug-Related AEs by SOC and toxicity[3]	Y											
Common Drug-related Grade 2-5 AEs [5]	Y											
Serious and other significant adverse events												
All SAEs by SOC	Y											
Reason for Considering as a Serious Adverse Event (FDA)				Y								
All Drug-Related SAEs by SOC	Y											
Fatal SAEs				Y								
Non-Fatal SAEs	Y			Y								
Drug-related non-fatal SAEs	Y											
Withdrawal AEs	Y			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	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
AEs, Fatal SAEs, and Drug-related SAEs (EudraCT)												
Cumulative AEs by visit	Y											
AEs by SOC and baseline 3rd agent	Y											
Suicidality assessment												
PSRAE				Y[7]								
Columbia suicidality (C-SSR)	Y			[18]								
Injection Site Reaction Adverse Events [14]												
ISR AEs (Event-Level) [20]	Y											
ISR AEs (Subject-Level) [21]	Y	Y										
ISR AEs (Subject-Level) by Visit and Severity [22]	Y	Y										
Maximum grade of ISR AEs (Subject-Level) by Needle Length [23]	Y											
Laboratory: Chemistry and Haematology												
Clinical Chemistry					Y							
%Lipids[24]					Y							
NCEP shifts in lipids		Y							Y			
Haematology					Y				Y			
Clinical Chemistry & Renal Biomarkers [13]					Y				Y			
Laboratory: Urinalysis (regardless of fasting status)												
Urine Dipstick	Y[9]			Y[8]								
Urine Concentration & Renal biomarkers[13]					Y							
Laboratory: Hepatobiliary												
Liver Assessment				Y [16]								
Hepatobiliary Abnormality criteria	Y[17]			Y								
Liver Chemistries				Y						Y[10]		
Laboratory: Markers												
Cardiovascular markers					Y[12]							

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
Bone markers					Y[11]							
ECG												
ECG findings	Y			Y								
ECG values					Y							
QTC	Y				Y				Y			
Other												
Vital Signs					Y							
Abacavir HSR				Y[15]								
Subjects who became Pregnant				Y								
Patient Profiles				[19]								
Skin Rash				Y								

NOTES :

- T = Table, F = Figures, L = Listings, 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. Refer to Section 13.6.2 for defining Extent of Exposure and adherence, refer to Section 13.1.1 for defining compliance
2. Includes reason for any dose change/interruption.
3. For AEs reported more than once by a subject, the most severe intensity will be included.
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. Common AEs are those with ≥5% incidence in either treatment group summarised by frequency.
6. Plots of incidence rates and relative risk with 95% CI for Q4W IM vs. Current ART.
7. Four PSRAE listings: Event and Description (Section 1 - Section 2), Possible Cause (Section 3), Section 4 and Section 5 - Section 8.
8. Listings for subjects with laboratory abnormalities for potential clinical concern, defined as any Grade1-4 toxicity, based on the DAIDs version described in Section 13.6.3 .
9. Shift table summarising baseline vs. maximum post-baseline result for urine dipstick protein.
10. Scatter plot of baseline vs. maximum post-baseline for ALT. Scatter plot of maximum ALT vs. maximum Bilirubin. Matrix plot of maximum liver chemistries.
11. Bone biomarkers including: Bone-specific alkaline phosphatase, procollagen type 1 N-propeptide, type 1 collagen cross-linked C-telopeptide, osteocalcin, 25 hydroxy-Vitamin D.
12. Cardiovascular biomarker : Glucose et al will be included in the summary of clinical chemistry, so there will be no separate summary for CV biomarkers
13. Renal biomarkers: Urine Retinol Binding Protein, Retinol Binding Protein Cystatin C. CKD-EP1 GFR using Cystatin C (derived in Section 13.6.3) will also be summarized
14. Repeat for CAB/RPV, CAB, RPV respectively.
15. Separate listings for exposure to abacavir, history of drug allergies, family conditions, skin rash, symptoms, vital signs, individual symptoms and diagnostic category assignment.
16. Separate listings for time of event: RUCAM score, biopsy, imaging, past/ current conditions and follow up
17. One summary of subjects and another table showing Subject Ids.
18. No lists are planned for eCSSR data.
19. Patient profiles are not planned. But it can be produced in adhoc way, as necessary.
20. Event-level summary: Percentages based on total number of ISR events within each treatment group including distribution of grade, duration, and event characteristics;

21. Subject-Level summary of characteristics of ISR AE (Overall and by Common ISRs); Percentage based on number of subjects within each treatment group; Includes distribution of grade and max grade, event characteristics, number of events per subject, rate of number of events per injection visit;
22. A corresponding plot of all grades and a separate plot of grade 3-5 events will be produced
23. Needle Length will be categorized into: <2 and ≥ 2 inch (please refer to Section 5.4 for the additional subgroup of ISR).
24. Please refer to Section 13.6.3 for defining percentage change from Baseline in Lipids

For the summary of Injection Site Reaction Adverse Events by Visit and Maximum Severity (Overall and by Common ISRs): ISRs will be assigned based on onset date to the most recent planned IM injection visit prior or equal to the AE onset date.

Maximum grade at each visit will be derived as the maximum grade among ISRs assigned to the particular visit, with consideration for whether the summary applies to a particular preferred term (vs. across preferred terms), drug-related associated to CAB and/or RPV, or stratification by subgroup (such as needle length).

Drug-related ISRs (based on investigator discretion) will be attributed to the causal agent (CAB vs. RPV) when this can be determined specifically based on the side of injection administration and the side of the reported ISR (as collected in the eCRF). If we are unable to determine the causal agent in those cases where both drugs are given on one side and the ISR is reported non-specifically, then the attribution to a specific causal agent will remain unknown.

Common ISR are defined as below:

Common ISR includes injection site pain, injection site induration, injection site nodules and any other ISR with ≥5% subjects (for Q4W arm only). The same set of common terms will be applied to 'overall' (CAB and/or RPV), CAB alone, RPV alone.

ISRs will be attributed to the needle length (<2, ≥2 inch) specifically based on the side of injection administration and the side of the reported ISR (as collected in the eCRF). If we are unable to determine the needle length in those events where both drugs are given on one side and their needle length are different, then the attribution to a needle length will remain unknown.

8.4.1. Planned safety statistical analysis

Statistical Analyses
Endpoints
• Change from baseline in bone markers at week 48
Covariates
• Treatment (Q4W IM, Current ART) • Stratified randomisation strata (sex at Birth, Baseline ART third agent class), age, and additional subgroup for bone marker (TDF at baseline, body mass index category, and smoking status). Please see details for defining these subgroups/covariates in Section 5.4.2
Data Handling
• All data remains as is (observed).
Model Specification
• Bone marker results will be log-transformed. The change in the log-transformed data at week 48 from baseline (i.e. log of ratio of post-baseline value over baseline value) for each bone marker will be analysed for the comparison between the two treatment arms. • An analysis of covariance (ANCOVA) model will be used with the above covariates. Age and Log-transformed biomarker at baseline will be included as continuous variables in the model and all other covariates will be included as categorical variables. • Interaction between treatment and ART third agent class and interaction between treatment and TDF at baseline will be examined, as described in the modelling steps below.
Model Results Presentation
• The estimated coefficients of the ANCOVA model will be transformed back (exponential transform) to reflect the change in the ratio of post-baseline value over baseline value rather than the change in the log ratio. The change in the ratio can then be translated into percent change from baseline (e.g. the ratio bb_{48}/bb_{bas} = 1.3 can be translated into 30% increase from baseline). • For each treatment, adjusted means of ratio and corresponding confidence intervals will be presented. • The adjusted difference of the ratio (post-baseline value)/(baseline value) between the two treatments with the corresponding confidence interval and *p*-value will be presented. • Modelling steps: 1. run separate statistical model with each interaction team at a time, i.e. each model including one interaction term and all covariates 2. run a joint model including any significant terms from step 1 and all covariates 3. If both interaction terms are included and significant in the joint model, the results will be presented by strata of third agent class X TDF at Baseline. 4. If only one interaction term is significant in the Joint model, the statistical model will be rerun by excluding the nonsignificant interaction term (if any). The results will be presented by strata of the one significant interaction factor (third agent class or TDF at Baseline). 5. If neither interaction term is significant, the statistical model will be rerun by excluding both interaction terms. The results will be presented for overall

Statistical Analyses
comparison between two arms. Note: Interaction term between treatment and third agent class and/or TDF at baseline is considered to be 'significant' at the level of <10%. .

9. PHARMACOKINETIC ANALYSES

The GSK Division of Clinical Pharmacology Modelling and Simulation (CPMS) will be responsible for the PK analysis of CAB. The Division of Global Clinical Pharmacology at Janssen Research and Development will be responsible for conduct or oversight of the PK analysis for RPV.

All PK and PK/PD displays will be based on the PK Population.

9.1. Primary Pharmacokinetic Analyses

9.1.1. Endpoint / Variables

A population-based PK analysis will be described under separate Population-PK Reporting and Analysis Plans. for CAB LA and RPV LA.

Table 6 provides an overview of the planned analyses based on CAB/RPV concentration data only with full details being presented in Section 13.13: List of Data Displays.

Table 6 Overview of Planned Pharmacokinetic Analyses

	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Pharmacokinetic [5]							
Plasma CAB concentration by Visit				Y[1][2	Y[1][3][4]	Y[3]	Y
Plasma RPV concentration by Visit				Y[1][2]	Y[1][3][4]	Y[3]	Y
Steady state concentration				Y[1]			
Pharmacokinetic/Pharmacodynamic							
CAB/RPV last trough and Week-8 concentration by Snapshot virologic Response				Y			
Analysis of Snapshot 'HIV-1 RNA≥50' at Week 48 by last trough CAB/RPV concentration, Week 8 trough concentration, and subgroup[6] – Univariate analysis /multivariate analysis	Y						
Individual CAB/RPV Concentration-Time Profiles for Subjects with HIV-1 RNA ≥ 50c/mL at Week 48					Y		

	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Last trough CAB/ RPV concentration and Week-8 trough concentration by snapshot 'HIV-1 RNA≥50' at Week 48					Y		
Change from baseline in 2hr post-dose QTc and 2hr post-dose CAB & RPV concentration at Week 4B, Week 48;						Y	
Maximum Change from Baseline(CFB) in ALT/Total Bilirubin versus Last Trough CAB/RPV Concentrations						Y	
Maximum Toxicity Grades of Most Frequently Reported AEs versus Last Trough CAB/RPV Concentrations						Y	

NOTES:

- T = Table, F = Figure, L = Listings, Y = 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. For both 'all' concentration and the 'evaluable' concentration. The evaluable concentration is derived from samples collected within pre-specified Time window (Section 13.6.5)
2. For both 'untransformed' and 'log –transformed' statistics.
3. The plots will be produced for the untransformed scale (i.e., a linear plot) and the log transformed scale (i.e., log-linear plot), separately.
4. Separate plots will be produced for Mean (SD) and Median concentration.
5. Standard summary statistics for concentration data will be calculated (i.e., mean, standard deviation, median, minimum and maximum). For Logarithmically transformed data, the summary statistics (i.e. geometric mean, coefficient of variation on geometric mean, 95% confidence interval for the geometric mean and standard deviation) will also be calculated.
6. Please refer to Section 5.4. i.e. randomisation strata, baseline and demographic factors, and additional subgroup for PK analysis

9.1.2. Planned Pharmacokinetic statistical analysis

Planned PK statistical analysis
Steady state concentration
Endpoints
• log_e-transformation of the Trough/Pre-dose plasma concentrations (CAB/RPV) on Week 16-48
Covariates
• Study Week
Data Handling
• All data remains as is (observed).
Model Specification
• A mixed effects ANOVA model will be fitted with Week (continuous variable) as a fixed effect and subject as a random effect for each analysis separately. The Kenward & Roger (KR) degrees of freedom approach will be used. The coefficient for the slope of the day effect on the log_e-scale will be used to evaluate steady state for each drug (CAB/RPV). The 90% confidence intervals for the slope for each treatment will be calculated. If it does not appear that steady-state has been demonstrated, early weeks (e.g. Week 16, 20, 24, etc...) results will be dropped

Planned PK statistical analysis
and the analysis repeated.
Model Checking & Diagnostics
• The Steady state will be claimed (the coefficient for the slope of the Week effect on the (natural) log scale was close to 0 or the 90% CI for the slope estimate included zero. If steady-state is not demonstrated, concentrations from early weeks (e.g. Week 16, 20, 24, etc...) dropped in sequence and the analysis repeated until either steady state shown or only two timepoints remain.
Model Results Presentation
• The coefficient for the slope of the day effect on the $\log_e$-scale, its Standard error and 90% interval will be presented.
Population PK Analysis
A population-based PK analysis will be done under separate Population-PK Reporting and Analysis Plans.
Exposure - antiviral activity analysis
Endpoints
Snapshot 'HIV-1 RNA≥50' at Week 48
Covariates
Randomisation strata (sex at Birth and baseline ART third agent class), demographic and Baseline characteristics (age -<50 vs ≥50, race, baseline CD4, baseline viral load, and baseline CDC subgroups), and additional subgroup/covariates for PK/PD efficacy analysis (last CAB/RPV trough concentration, CAB/RPV trough concentration at nominal visit of Week 8, Baseline BMI, length of injection needle). Please see details for defining these subgroups/covariates in Section 5.4.2.
Data Handling
• All data remains as is (observed).
Model Specification
Logistic regression will be used to exam the correlation between the endpoint (Snapshot 'HIV-1 RNA≥50') at Week 48 and the covariates/subgoups. CAB/RPV trough concentration will be included in the models as continuous variables. This logistic regression analysis will be performed for each covariate, separately (univariate analysis), and will also be performed with one multivariate analysis using *Backward* stepwise selecting approach to identify the covariates potentially affecting virologic response.
Model Checking & Diagnostics
For the multivariate analysis, a logistic regression model that best predicts the dependent variable (i.e. 'HIV-1 RNA≥50') from the independent variables (i.e. covariates/factors with P<0.15 from univariate analysis) will be determined using the backward stepwise selecting approach. The last trough and Week-8 trough PK concentrations will be logarithmically transformed with base of 2. The analysis will start with all covariates in the model and remove a covariate with the largest p-value (i.e. the least statistically significant) each time and continue until the stopping rule is reached

Planned PK statistical analysis
when all remaining covariates have p-value <15%.
Model Results Presentation
• The odds ratio, 95% confidence interval, and P value will be presented. Estimated effect represents the change in log odds for a two-unit increase in the pk concentration

10. HEALTH OUTCOMES ANALYSES

10.1. Endpoint / Variables

- Change from Week 5 in Dimension Scores and proportion of participants considering pain and local reactions following injection using PIN (Perception of iNjection Questionnaire),
- Change from Baseline in HR QoL,
- Change from Baseline in health status using SF-12,
- Change from Baseline in treatment acceptance using ACCEPT, Change from Week 4b in tolerability of injection,
- Change from baseline in total "treatment satisfaction" score, and individual item scores of the HIV Treatment Satisfaction Status Questionnaire (HIVTSQs).

10.2. Summary Measure

Mean treatment difference (Q4W – Current ART) at visits of interest through to Week 48 (i.e. the assessment visits detailed in Table 7).

10.3. Population of Interest

The primary health outcomes analyses will be based on the Intent-to-Treat Exposed population, unless otherwise specified.

10.4. Strategy for Intercurrent (Post-Randomization) Events

If a participant discontinues treatment prior to the timepoint of interest such that there is no evaluable on-treatment assessment for the timepoint of interest (see Table 20 for definition of on-treatment), the data will be computed or imputed (see Section 13.6.6)

10.5. Statistical Analyses / Methods

Table 7 provides an overview of the planned analyses. Details of the planned displays are provided in Appendix 13: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Table 7 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
Perception of Injection (PIN) at Week 5, 41, 48, 96														
Individual Item Scores				Y			Y							
Domain of 'Bother from injection site reactions', 'Leg movement', 'Sleep', 'Acceptability'	Y[4]			Y			Y				Y			
Health-related quality of life (HATQoL) at baseline, wk24, 48, 96, withdrawal														
Individual Item Scores				Y			Y							
Subscale of Life satisfaction, HIV medication, and disclosure worries				Y			Y	Y	Y[1]		Y			
Health Status (SF-12) at Baseline, wk24, 48, 96)														
Individual Item Scores				Y			Y							
Total Score, Mental health component (MCS) and physical component summary (PCS)[2]				Y			Y	Y	Y[1]		Y			
Treatment Satisfaction Score (HIVTSQs) at Baseline, Week 4b, 24, 44, 96, withdrawal														
Individual Item Scores				Y			Y							
Individual Item Scores by subgroup[3]				Y										
Treatment Satisfaction Score				Y			Y	Y	Y[1]		Y			
Treatment Satisfaction Score Change (HIVTSQc) at 48, withdrawal														
Individual Item Scores	Y			Y			Y							
Treatment Satisfaction Score Change	Y			Y			Y							

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Treatment Acceptance (ACCEPT) at Baseline, week 8, 24, 48, 96, withdrawal														
proportion of Individual item score				Y			Y							
Acceptance/General Dimension Score				Y			Y	Y	Y[1]		Y			
Tolerability of injection (NRS) at week 4b, week 5, 40, 41, 96 within Q4W IM arm														
proportion of Individual item score				Y			Y							
Tolerability Score (Q4W IM only)				Y			Y				Y			
Treatment Preference at Week 48 (for both treatment arms) and Week 96 (for Current ART only)														
Treatment: Monthly injection vs Daily oral ART				Y			Y							
Willingness to switch at Baseline (Q4W IM), and Week 52 (Current ART)														
Willingness to switch				Y			Y							

1. Line Plot of Adjusted Mean (95% CI) for each treatment arm, as well as the adjusted mean difference (95%CI) between the two treatment arms (if questionnaire was used for both arms during maintenance phase).
2. Component scores will be calculated form Computer Software purchased from QualityMetric.
3. Please refer to Section 5.4 (i.e. randomized strata, demographic and baseline subgroup)
4. Wilcoxon Signed -rank test for analysis of 'Acceptance' only with p-value reported

10.6. Planned Health Outcomes Statistical Analyses

Statistical Analyses
Endpoints
Change from Baseline in ○ HIVTSQs total treatment satisfaction score at Week 4b, 24, 44 ○ ACCEPT general acceptance score at Week 8, 24, 48 ○ SF-12: Total Score, physical component summary(PCS) and mental component summary(MCS) at week 24, 48 ○ HATQoL (Life satisfaction, HIV medications, disclosure worries) at week 24, 48.
Model Specification
• An analysis of covariance (ANCOVA) model will be used at each visit at Maintenance phase with covariates: treatment, age (<50, ≥ 50), baseline third agent class, sex at birth, and race (i.e. white, non-white) (as described in 5.4) and baseline score value (as a continuous

variable).
- Adjusted point estimates will be derived as LSMEAN S using the observed margins (OM) option within PROC MIXED in SAS.
- No adjustment for multiplicity will be applied as these analyses will be considered exploratory.
- Interactions between treatment and each of the covariates will not be assessed unless the exploratory subgroup analyses on the primary endpoint highlights significant interactions. In this situation, the interaction(s) of interest will be assessed and, if necessary, results will be reported in the clinical study report. Interactions between treatment and the baseline score will be investigated but not included in the model. If interactions are found to be significant, results might have to be presented separately by subgroup.
- No adjustment for multiplicity will be applied as these analyses will be considered exploratory.

Dataset

- LOCF dataset will be used.

Model Results Presentation

- Adjusted treatment difference (Q4W IM – Current ART), its 95% CI and the associated p-value. The interaction between treatment and the baseline score will be included in a footnote.
- Plots of adjusted mean change from baseline (95% CI) for each treatment group, and the adjusted mean difference (95%CI) between the two treatment arms from the model will be generated across visit.

Statistical Analyses

HIVTSQc

- **Treatment Satisfaction Score (Change) at Week 48**

Model Specification

- An analysis of variance (ANOVA) model will be used with covariates: treatment, age (<50, ≥ 50 years old), baseline third agent, sex at birth, and race (white, non-white) (as described in Section 5.4)

Dataset

- The observed case (OC) dataset uses only the data that is available at Week 48, with no imputation for missing values.

Model Results Presentation

- Adjusted means, 95% CI, and associated P value will be presented for the treatment difference (Q4W IM –Current ART). Adjusted point estimates will be derived as LSMEAN S using the observed margins (OM) option in modelling.

11. VIROLOGY

The virology analyses will be mainly for the CVF populations using genotype and phenotype data based on plasma sample, unless otherwise specified.

Table 8 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 13: List of Data Displays.

Table 8 Overview of Planned Virology Analyses

Endpoint	Absolute			
	Summary		Individual	
	T	F	F	L
Genotypic resistance at time of CVF[1]				
Prevalence of genotype	Y[2]			
On Treatment mutation	Y[2]			
Phenotypic resistance at time of CVF[1]				
Prevalence of phenotype	Y[3]			
Fold change for CAB and RPV	Y			
IN, PR/RT replication capacity				Y
Other				
Genotypic and phenotypic data on the last on-treatment isolates in subjects with HIV-1 RNA ≥200 c/mL	Y			

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

1. For the CVF as indicated by two consecutive plasma HIV-1 RNA levels ≥200 c/mL after prior suppression to <200 c/mL, the first visit of these two consecutive visits is defined as 'the suspected visit', and the 2nd one is the confirmed visit. 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. If the test fails with the sample at the suspected visit, we will just report it as 'no data'. The sample from the confirmed visit will not be tested for resistance.
2. No. and percentage of subjects with IN resistance mutations or major mutations in the classes of NNRTI, NRTI, PI, respectively
3. Separate outputs by phenotypic cut-off and by number of drugs to which subjects are resistant.

Additional analyses for HIV-1 resistance may be carried out on peripheral blood mononuclear cell (PBMC) samples collected at Baseline for CVF subjects.

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13. APPENDICES

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Section 13.13	Appendix 13: List of Data Displays
Separate document	Example Mock Shells for Data Displays

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

13.1.1. Exclusions from Per Protocol Population

Important protocol deviations leading to exclusion from Per Protocol population are those deviations which may

i. directly impact the efficacy endpoint of HIV-1 RNA; or

ii. 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 (e.g. Week 48/96), 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. A final 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 based on case-by-case clinical determination:

Number	Exclusion Description
01	Subject deviates from inclusion or exclusion criteria that may significantly affect exposure, response to therapy or subject safety or that are fundamentally inconsistent with the intended study population, as recorded in the Protocol Deviation form in the eCRF based on study team review (where indicated in the PDMP as case-by-case determination).
02	Subject has non-compliance with IP (including IM dosing errors) or took/received incorrect IP (i.e., other than the one to which they were randomized) that is: Maintenance phase 1. > 10% of total time on-treatment with under dosing deviations up to the analysis timepoint of interest (e.g. Week 48). 2. Two or more injection intervals affected by **over dosage** deviations (e.g. extra injection or excessive volume administered, length of time between injections less than 3 weeks, excluding split doses) up to the analysis timepoint of interest. For this purpose, the total number of **non-compliant** under dosing days up to the analysis timepoint of interest, is derived as follows: • Control Arm: a. Interruptions of control arm ART for reasons other than treatment-related adverse events/laboratory abnormalities (based on concomitant ART eCRF forms); • Q4W IM Arm: a. Length of time until next injection from date of dosage/administration deviation potentially resulting in under dosage (e.g. 1ml administered instead of 2ml) b. Length of time between injections exceeding 5 weeks (e.g. missed or late

Number	Exclusion Description
	injection visit) for post Week 12 and exceeding 4 weeks for Week 8 and Week 12 c. Interruptions of oral lead-in or oral bridging (if necessary) for reasons other than treatment-related adverse events/laboratory abnormalities (based on eCRF Exposure forms); Note: The total no. of under dosage non-compliance days will be derived based on the above rules and censored at the date of last on-treatment viral load for the visit of Week 48 snapshot analysis during Maintenance phase.
03	Prohibited medications: receiving ART medication other than that prescribed/allowed by the study (excluding permanent changes in ART regimen; such cases will be retained as 'HIV1-RNA≥50 c/mL' in the per protocol snapshot analysis) or receiving prohibited concomitant medication that would impact exposure or response to therapy with duration and route of administration taken into consideration, as recorded in the Protocol Deviation form in the eCRF based on study team review (where indicated in the PDMP as case-by-case determination)
04	Permanent discontinuation of IP/withdrawal due to a reason of "Protocol Deviation" (as recorded in the eCRF Conclusion form).
05	Other important protocol deviations that exclude subject from Per protocol population as recorded in the Protocol Deviation form in the eCRF based on study team review (where indicated in the PDMP as case-by-case determination).

Non-compliance Rate (under dosage deviation)

The rate of under dosage non-compliance for each subject will be derived based on the total number of days impacted by under dosage deviations up to analysis timepoint of interest (e.g. for Week 48 analysis, the analysis timepoint of interest is the date of Last on-treatment viral load for the visit of Week 48 Snapshot analysis), against the total no. of intended exposure days up to the same timepoint, see the example below for Week 48 analysis.

Total no. of intended exposure days =Date of Last on-treatment viral load* - Date of treatment start at Maintenance phase +1

*last on-treatment viral load is the viral load used for snapshot analysis at week 48.

Non-compliance (under dosing) rate= total no. of under dosage non-compliance days /total no. of intended exposure days * 100

13.2. Appendix 2: Schedule of Activities

13.2.1. Protocol Defined Schedule of Events

Procedure	Screening Visit[a]	Maintenance Phase											Extension Phase								Withdrawal	Follow-up Phase
		Week																				
		Baseline, Day 1	4A	4B[b]	5[b]	8, 12,16,20	24	28, 32, 36,40	41[b]	44	48	52	56A	56B[b]	60	64, 72, ,80, 88	68, 76, 84, 92	96	Every 4 Weeks After Week 96	Every 12 Weeks After Week 96		
Clinical and Other Assessments																						
Written informed consent	X																					
Eligibility Verification (Inclusion/Exclusion Criteria)	X	X[c]									X[c]											
Randomization		X																				
Demography	X																					
Medical History[d]	X																					
Medication History/ Prior ART history	X																					

Procedure	Screening Visit[a]	Maintenance Phase										Extension Phase								Withdrawal	Follow-up Phase
		Baseline, Day 1	Week																		
			4A	4B[b]	5[b]	8, 12,16,20	24	28, 32, 36,40	41[b]	44	48	52	56A	56B[b]	60	64, 72, ,80, 88	68, 76, 84, 92	96	Every 4 Weeks After Week 96	Every 12 Weeks After Week 96		
Symptom Directed Physical Exam and Medical Assessment[e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight, Height and BMI[f]		X									X			X				X			X	
Cardiovascular risk assessment	X	X																				
Vital Signs (BP, HR,Temperature)[g]	X	X									X			X				X			X	
12-lead ECG [h]	X	X pre-dose x3		X							X			X				X			X	
CDC HIV-1 classification	X	X																				
HIV Associated Conditions			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Procedure	Screening Visit[a]	Maintenance Phase										Extension Phase								Withdrawal	Follow-up Phase
		Week																			
		Baseline, Day 1	4A	4B[b]	5[b]	8, 12,16,20	24	28, 32, 36,40	41[b]	44	48	52	56A	56B[b]	60	64, 72, ,80, 88	68, 76, 84, 92	96	Every 4 Weeks After Week 96	Every 12 Weeks After Week 96	
AEs, SAEs, Concomitant Medications	X[i]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ISR Assessment				X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X
Columbia Suicide Severity Rating Scale (eC-SSRS) [j]	X	X	X			X	X	X		X	X				X	W 72	W 84	X			X	
Clinical chemistry and Haematology	X	X	X			X	X	X		X	X	X	X		X	X		X		X	X	X
Rapid Plasma Reagin (RPR)	X	X																				
Pregnancy Testingk	SR	UR	SR	UR		SR	SR	SR		SR	SR	SR	SR	UR	SR	SR	SR	SR	SR	SR	SR	SR
HIV-1 RNA and sample for storage[l] (S)=Storage only	X	X		X		X	X	X		X	X	S		X	X	X		X		X	X	X

Procedure	Screening Visit[a]	Maintenance Phase											Extension Phase								Withdrawal	Follow-up Phase
		Week																				
		Baseline, Day 1	4A	4B[b]	5[b]	8, 12,16,20	24	28, 32, 36,40	41[b]	44	48	52	56A	56B[b]	60	64, 72, ,80, 88	68, 76, 84, 92	96	Every 4 Weeks After Week 96	Every 12 Weeks After Week 96		
CD4+ cell count	X	X		X		X	X	X		X	X	X		X	X	X		X		X	X	X
CD8+ cell count		X		X			X				X			X				X			X	
Urinalysis[m]		X	X				X				X		X					X			X	
Fasting Lab Assessments: Glucose, Cholesterol (Total, HDL and LDL) and Triglycerides[n]		X									X										X[o]	
Hepatitis B (HBsAg), Anti-HBc, and Anti-HBsAG, Hepatitis C (anti-HCV Ab)	X																					
HLA-B*5701	X																					
PT/PTT/INR	X	X																				

Procedure	Screening Visit[a]	Maintenance Phase										Extension Phase								Withdrawal	Follow-up Phase
		Week																			
		Baseline, Day 1	4A	4B[b]	5[b]	8, 12,16,20	24	28, 32, 36,40	41[b]	44	48	52	56A	56B[b]	60	64, 72, ,80, 88	68, 76, 84, 92	96	Every 4 Weeks After Week 96	Every 12 Weeks After Week 96	
Renal, bone, marker analytes (blood/urine)[p]		X									X							X				
PBMCs[q]		X																X			X	
Genetics sample[r]		X																				
Pharmacokinetics – CAB + RPV only																					
PK sampling[s] (S)=Storage only				X	X	X	X	X	X	X	X	X		X	X	S		X			X	S
Investigational Products																					
Oral CAB and Oral RPV Dispensation[t]		X	X									X	X									
IP accountability (Pill Counts)			X	X									X	X								

Procedure	Screening Visit[a]	Maintenance Phase											Extension Phase								Withdrawal	Follow-up Phase
		Week																				
		Baseline, Day 1	4A	4B[b]	5[b]	8, 12,16,20	24	28, 32, 36,40	41[b]	44	48	52	56A	56B[b]	60	64, 72, ,80, 88	68, 76, 84, 92	96	Every 4 Weeks After Week 96	Every 12 Weeks After Week 96		
IM treatment administration[u]				X		X	X	X		X	X	X	X	X	X	X	X	X	X	X		
Patient Reported Outcomes[v]																						
HAT-QoL (short-form)		X					X				X							X			X	
SF-12		X					X				X							X			X	
HIV TSQs		X		X			X			X								X			X	
HIV TSQc[w]											X										X	
ACCEPT		X				X Wk8 only	X				X							X			X	
Reason for Switch[x]		X										X										
Preference[y]											X							X				

Procedure	Screening Visit[a]	Maintenance Phase										Extension Phase								Withdrawal	Follow-up Phase
		Week																			
		Baseline, Day 1	4A	4B[b]	5[b]	8, 12,16,20	24	28, 32, 36,40	41[b]	44	48	52	56A	56B[b]	60	64, 72, ,80, 88	68, 76, 84, 92	96	Every 4 Weeks After Week 96	Every 12 Weeks After Week 96	
NRS[z]				X	X			X Wk40 only	X									X			
PIN					X				X		X							X			X	
Follow Up Visit: Conduct approximately 4 weeks after the last dose of IP. Required only if the participant has ongoing AEs or lab abnormalities at the last on-study visit. This visit may be conducted by telephone.																					

a. Complete all Screening assessments within 35 days. Participants may begin the Maintenance Phase as soon as all Screening assessments are complete. Participants may be rescreened once and will be assigned a new participant number.
b. Visits at Weeks 4b, 5, 41, and 56b are only for participants randomized to CAB LA + RPV LA or transitioning from current ART to CAB LA + RPV LA during the Maintenance or Extension Phase, respectively.
c. Confirmation of eligibility to enter the Maintenance Phase, and eligibility to enter the Extension Phase.
d. Collect full routine medical history plus (report at Baseline visit): HIV risk factors (may be collected at a later study visit), cardiovascular risk factors (assessments include smoking status and history, family history of cardiac events), recent [≤6 months] illicit drug use, intravenous drug use, gastrointestinal disease, metabolic, psychiatric, renal, bone, and neurologic disorders.
e. Physical exams should be conducted as part of normal routine clinical care but data will not be collected in the eCRF. Medical assessments include any decisions the study staff must make for participants management and/or care of participant.
f. Height collected at Baseline only.
g. Measure vital signs after about 5 minutes of rest in a semi-supine position.
h. A 12-lead ECG will be performed after resting in a semi-supine position for at least 5 minutes. ECGs will be performed pre-dose. ECG will be perfomed in triplicate at Baseline (Day 1). In addition to a pre-dose ECG, a 2-hour post-dose ECG will be performed at Weeks 4B and Week 48 for subjects randomized to CAB LA + RPV LA only.
i. Only SAEs related to study participation or to a concomitantly administered ViiV/GSK product will be collected between obtaining informed consent and administration of study drug at Day 1.

j. On Day 1, the eC-SSRS is to be administered prior to randomization. The eC-SSRS will be administered at each Q4W injection visit through the Week 48 primary endpoint, followed by Q12W thereafter through Week 96 (Week 60, 72, 84, 96). The eC-SSRS will preferably be completed at the beginning of the visit following administration of other PROs required prior to injections.
k. Women of childbearing potential only. SR=serum, UR=urine. Pregnancy events will be captured starting at Day 1 following exposure to study drug. Serum pregnancy test can substitute for urine pregnancy test if locally required but must be appropriately timed to confirm pregnancy status prior to randomization and first IM administration.
l. HIV-1 RNA will not be collected for analysis at Week 52 and Week 100 (Week 48 or Week 96 retest will be captured as unscheduled visit). Plasma for storage will be collected at Week 52 and Week 100. Plasma for storage samples will be used for possible future analyses
m. A morning specimen is preferred. To assess biomarkers: urine albumin/creatinine ratio; urine protein/creatinine ratio; and urine phosphate.
n. An overnight fast is preferred; however, a minimum of a 6-hour fast is acceptable.
o. Only collect if the Withdrawal visit occurs at Week 48, or 96.
p. Blood sample for renal and bone biomarker assessments: **Renal:** Cystatin C; Retinol Binding Protein (RBP); **Bone:** bone specific alkaline phosphatase, procollagen type 1-N-propeptide, type 1 collagen cross-linked C-telopeptide, osteocalcin, 25 hydroxy-Vitamin D
q. Whole blood/PBMC collection samples may be used for virologic analyses. PBMCs will be collected at Day 1, Week 96, and Withdrawal if prior to Week 96.
r. Informed consent for genetic research must be obtained before sample collection
s. One blood sample for CAB and RPV each to be collected at each PK timepoint. PK samples are to be collected pre-dose during visits requiring IM administration. 2-hour post dose samples also taken at Weeks 4b, 48, 56b, and 96. Pre-dose samples at Weeks 56b, 60, and 2 hour post-dose sample at Week 56b are only for subjects transitioning from Current Art arm to CAB LA + RPB LA. Pre-dose samples are to be collected after review of PK diary at Week 4b and 56b and prior to the final oral dose of CAB + RPV. Additionally, PK samples will be taken during the 1-week post-dose Week 5 and 41 visits. PK window allowed for sample collection; includes 3 to 10 days for 1-week post dose sample (Visits 5 and 41); ±one hour for 2-hour post dose sample (Weeks 4b, 48, 56b, and 96).
t. Only for Participants entering CAB LA+ RPV LA Oral Treatment
u. Participants switching to CAB LA + RPV LA will take final dose of oral lead-in regimen in the clinic at The Week 4b visit or Week 56b and begin injections. If possible, injections should be spaced approximately 2 cm from one another and from the site of any previous injection and or any injection site reaction. Bring RPV LA to approximately room temperature prior to injecting. Time and location of injection (right or left) as well as needle length used will be collected in the eCRF. The first injection can be performed as soon as central lab results become available and safety parameters are reviewed.
v. With the exception of the NRS, all Patient Report Questionnaires/Surveys are recommended to be administered at the beginning of the visit before any other assessments are conducted and prior to administration of the NRS is to be given post injection. Conduct questionnaires/surveys at Withdrawal if occurring prior to Week 96.
w. HIV TSQ (c) to be administered at Week 48 to LA injection arm only
x. "Reason for switch" will be administered prior to randomization at Day 1. At Week 52, "Reason for Switch" will be given only to participants randomized to the "Current ART" arm.
y. Preference" question to be administered at Week 48 to patients randomized to CAB LA + RPV LA arm, and at Week 96 to patients randomized to the "current ART arm" who switched to CAB LA + RPV LA at the end of maintenance phase.
z. NRS will be administered on injection visits approximately 30-60 minutes following injections. Participant should record the maximum level of pain experienced with the most recent injections.

Note: BP – Blood pressure, HR – Heart Rate, HDL – High Density Lipoprotein, LDL – Low Density Lipoprotein, PT Prothrombin Time, PTT Partial Thromboplastin Time,INR International normalized ratio

13.3. Appendix 3: Assessment Windows

13.3.1. Definitions of Assessment Windows for Analyses

Laboratory data, vital signs, ECGs, health outcomes assessments, and genotypic/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.

In most cases the window around an assessment will include all dates from the midpoints between the target day and that of the previous and the proceeding visits. In general, the nominal target study day for week *w* is (7**w*) +1.

For parameters which are not scheduled to be assessed at particular visits, the all-inclusive assessment windows will still be used; however, 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 any algorithms that make use of additional data (e.g., Snapshot).

Prior to visit slotting, assessments are first assigned to a study phase (screening, maintenance, extension, or Long Term Follow Up) based on the Tables in Section 13.4.1 and treatment state based on Section 13.4.2.

Maintenance phase assessments are assigned based on the Maintenance Phase Study Day as shown in Table 9. The analysis visits from Week 4 to Week 52 should be only applied to the assessments that are already assigned to Maintenance phase (on-treatment). Extension phase assessments are assigned based on the Maintenance Phase Study day for subjects continuing Q4W IM dosing into the Extension Phase, and based on the Extension Phase Study Day for subjects switching from the control arm to Q4W IM dosing for the Extension phase as shown in Table 10. The analysis visits from Week 56 (except for Follow-up) in the Extension phase should be only applied to the assessments that are already assigned to Extension phase (on-treatment).

Long-term Follow-up phase assessments are assigned based on the LTFU study day as shown in Table 12. The analysis visits in LTFU should be only applied to the assessments that are already assigned to LTFU phase regardless of treatment state. See Section 13.6.1, for derivation of Maintenance, Extension and LTFU Study Day.

13.3.2. Definitions of Assessment Windows for Data Other than Health Outcome and PK

Table 9 Assessment Windows for Screening & Maintenance Phase Data

Parameters[d] collected in sparse visit [c]	Analysis Window	Target Study Day	Analysis Timepoint
	Study Day ≤1 (the first record if there are multiple values)	The day of earliest record	Screening
	Last available recorded value up to and	1	Baseline

Parameters[d] collected in sparse visit [c]	Analysis Window	Target Study Day	Analysis Timepoint
	including the date of first maintenance phase dose of IP		
ECG, CD8, CD4/CD8 ratio	2 ≤ Study Day ≤ 70	29	Week 4
	2 ≤ Study Day ≤ 42		
	43 ≤ Study Day ≤ 70	57	Week 8
	71 ≤ Study Day ≤ 98	85	Week 12
	99 ≤ Study Day ≤ 126	113	Week 16
	127 ≤ Study Day ≤ 154	141	Week 20
urinalysis, CD8, CD4/CD8 ratio	155 ≤ Study Day ≤ 210	169	Week 24
	155 ≤ Study Day ≤ 182		
	183 ≤ Study Day ≤ 210	197	Week 28
	211 ≤ Study Day ≤ 238	225	Week 32
	239 ≤ Study Day ≤ 266	253	Week 36
	267 ≤ Study Day ≤ 294	281	Week 40
	295 ≤ Study Day ≤ 322	309	Week 44
ECG, CD8, CD4/CD8 ratio, urinalysis, lipids, bone and renal markers	323 ≤ Study Day ≤ 378	337	Week 48
	323 ≤ Study Day ≤ 350		
	For 'Current ART' arm; 351 ≤ Study Day ≤ Maintenance Current ART Stop Day[b] + 1 For 'Q4W' arm: 351≤ Study Day ≤ Max (Day of Last Q4W IM Dose + 35, Last Oral dose Day + 1) [a]	365	Week 52
	For subjects who discontinued from oral lead-in during Maintenance phase, Study Day > (Day of last oral lead-in dose+1) Subjects discontinued from Current ART and not continuing into extension phase Study Day > (Maintenance Current ART Stop Day[b] +1)		Follow-up

[a] Last Q4W IM / last oral dose is only applied to subjects who permanently discontinue from study treatment

[b[Current ART stop day: the last permanently stop day among all ARTs taken during Maintenance phase.

[c] For parameters with sparse collection, post baseline data will only be slotted to those specific analysis windows. The Screening or Baseline slotting will be based on the same rules as all other lab parameters use.

[d] **Urinalysis**: Urine Albumin/Creatinine, Urine Creatinine, Urine pH, Urine Protein/Creatinine, Urine Erythrocytes, Urine Specific Gravity, Urine Leukocytes, Urine Retinol Binding Protein, Urine Phosphate, Urine Creatinine

Bone marker: Bone Specific Alkaline Phosphatase, Osteocalcin, Procollagen 1 N-Terminal Propeptide, Vitamin D, Type I C-Telopeptides

Renal marker: Cystatin C, Retinol Binding Protein

Lipids: Cholesterol, HDL Cholesterol Direct, LDL Cholesterol Calculation, LDL Cholesterol Direct, Total Cholesterol/HDL Cholesterol Ratio, Triglycerides

Table 10 Assessment Windows for Extension Phase for Data Other than Health Outcome and PK

Analysis Set / Domain	Parameter (if applicable)	Target Extension Phase Study Day	Target Study Day	Analysis Window	Analysis Timepoint
Subjects Continuing Randomized Q4W IM Regimen					
All	All		393	Study day of Nominal Week 52 visit +1 ≤ Study Day ≤ 406	Week 56
			421	407 ≤ Study Day ≤ 434	Week 60
			449	435 ≤ Study Day ≤ 462	Week 64
			505	463 ≤ Study Day ≤ 532	Week 72
			561	533 ≤ Study Day ≤ 588	Week 80
			617	589 ≤ Study Day ≤ 644	Week 88
			673	645 ≤ Study Day ≤ 714	Week 96
			7*w + 1	(7*w - 41) ≤ Study Day ≤ (7*w + 42)	Week w w = 108, 120, 312, 144,…
Subjects Switching to Q4W IM Dosing					
		1		Last available recorded value up to and including the date of first Extension phase dose of IP	Extension Baseline
		29		2 ≤ Extension Study Day ≤ 42	Week 56 #
		57		43 ≤ Extension Study Day ≤ 70	Week 60
		85		71 ≤ Extension Study Day ≤ 112	Week 64
		141		113 ≤ Extension Study Day ≤ 168	Week 72
		197		169 ≤ Extension Study Day ≤ 224	Week 80
		253		225 ≤ Extension Study Day ≤ 280	Week 88
		309		281 ≤ Extension Study Day ≤ 350	Week 96 #
		7*(w-52) + 1		(7*(w-52) - 41) ≤ Study Day ≤ (7*(w-52) + 42)	Week w w = 108,

Analysis Set / Domain	Parameter (if applicable)	Target Extension Phase Study Day	Target Study Day	Analysis Window	Analysis Timepoint
					120,…
			For subjects who discontinued from oral lead-in during extension phase: Study Day >Day of last oral lead-in dose +1	Follow-up	

NOTES:

- For parameters which are not scheduled to be assessed at particular visits, the all-inclusive windows defined will still be used.
- Assessments at unscheduled visits will be included for 'any time On-treatment' time points and in data listings, as well as algorithms that make use of additional data (e.g., Snapshot).
- Nominal Week 52 visit is the original visit from eCRF (i.e. the VISIT variable as opposed to AVISIT)

[#] For ECG, the reporting analysis visits will be at Week 56 and Week 96 only, the upper bound of window will be expanded to +6 weeks for each analysis visit, i.e. analysis window for Week 56 is 2 ≤ Extension Day ≤ **70**, for Week 48 is 281 ≤ Extension Day ≤ **378**

Table 11 Assessment Windows for Summary of Snapshot Data (Window at Key Analysis Time points) — Data assigned to Maintenance Phase Only

Day of Assessment	Reporting Assessment Window	Snapshot Windows
155 ≤ Study Day ≤ 182 (if there is no data, then expanded to 127≤ Study day≤210) (This window extension is for IDMC report only. For other deliveries including primary Week 48, it remains to be 155 ≤ Study Day ≤ 182)	Week 24	± 2 Weeks, if no data, expanded to ± 6 weeks
295 ≤ Study Day ≤ 378	Week 48	± 6 Weeks
Note1: Snapshot analysis window for other visits will be based on Table 9. Note2: Apply Snapshot analysis windows only to viral load data that is on-treatment (per Table 20) within the Maintenance phase (Per Table 17)		

Table 12 Assessment Windows for Summaries of Long-Term Follow Up Phase Data for Subjects Who Received at Least One Injection of CAB+RPV and Permanently Discontinued from Study Treatment

Day of Assessment	Assessment Window	Target Study Day of Window
1 ≤ LTFU Study Day ≤ 60	LTFU Month 1	30
61 ≤ LTFU Study Day ≤ 135	LTFU Month 3	90
136 ≤ LTFU Study Day ≤ 225	LTFU Month 6	180
226 ≤ LTFU Study Day ≤ 315	LTFU Month 9	270
316 ≤ LTFU Study Day ≤ 405	LTFU Month 12	360
(30*m - 44) ≤ LTFU Study Day≤ (30*m + 45)	LTFU Month m m = 15, 18,21,…	7*m
An assessment may be slotted to both LTFU and Maintenance /Extension Phase		

13.3.3. Assessment Window for Study Conclusion

The 'Phase conclusion' records in disposition data will be slotted based on Table 9 and Table 10. However, for the record of 'Phase Conclusion', if a discontinuation date is post-treatment, then it will be slotted to the last on-treatment visit within the same treatment phase rather than follow up.

13.3.4. Assessment Window for Health Outcome Data

13.3.4.1. NRS

NRS questionnaire assessments are assigned to analysis visits based on the windows defined in Table 13.

Table 13 Assessment Windows for Maintenance Phase NRS Questionnaire Data

Domain	Parameter	Target Date	Analysis Window	Analysis Timepoint
NRS	All	Date of 1st Injection	Assessment Date ≤ Date of 1st injection + 2	Week 4
		Date of 1st injection+7	Date of 1st injection +3 ≤ Assessment Date ≤ Date of 1st injection + 42	Week 5
		Date of W40 Injection	**If participant received Week 40 injection:** Date of WK40 injection - 42 ≤ Assessment Date ≤ Date of W40 Injection + 2	Week 40
		Date of 1st Injection + 252	**If participant did not receive Week 40 injection:** Date of 1st injection + 210 ≤ Assessment Date ≤ Date of 1st injection + 280	

Domain	Parameter	Target Date	Analysis Window	Analysis Timepoint
		Date of W40 Injection + 7	**If participant received Week 40 injection:** Date of W40 Injection + 3 ≤Assessment Date ≤ Date of W40 Injection + 28	Week 41
		Date of 1st Injection + 308	**If participant received Week 40 injection:** Date of 1st Injection + 280 < Assessment Date ≤ Date of 1st Injection + 350 **AND** Assessment Date > Date of WK40 injection + 28	Week 48
		Date of 1st Injection + 308	**If participant did not receive Week 40 injection:** Date of 1st Injection + 280 < Assessment Date ≤ Date of 1st Injection + 350	
Note: Apply NRS analysis windows only to assessments that are on-treatment (per Table 20) within the Maintenance phase (Per Table 17)				

13.3.4.2. PIN/HATQoL/SF-12/HIVTSQs/HIVTSQc/ACCEPT/Treatment Preference

PIN, HATQoL, SF-12, HIVTSQs, HIVTSQc, ACCEPT, Treatment Preference, Willing to Switch questionnaire assessments will be assigned to analysis visits as follows: Baseline: Baseline will be defined as last available recorded value up to and including the date of first maintenance phase dose of study treatment.

Post-Baseline nominal visit: There will be no slotting for Post-baseline planned nominal visits (i.e. analysis visit =visit). The post-baseline planned nominal visits for each questionnaire are listed in Table 14.

Withdrawal/unscheduled post-baseline visit at Maintenance phase (per Table 17) will be slotted per the following slotting steps:

- Identify the 'last nominal visit' with the HO assessment performed prior to the unscheduled/withdrawal visit to be slotted during the Maintenance phase
- The unscheduled/withdrawal visit will be slotted to the planned nominal visit subsequent to the 'last nominal visit' during the Maintenance phase

Example 1, for HATQoL, the post-baseline planned nominal visits are Week 24, 48, and 96. If a subject has the 'last nominal visit' (with HATQoL assessment) at Week 24 prior to withdrawal at Week 36, the withdrawal assessment will be slotted to the subsequent planned nominal visit of Week 48.

Example 2, for HATQoL, if there is unscheduled visit between Week 24 and Week 48. This unscheduled visit will be slotted to Week 48 per the rule. In this case, there are two assessments with analysis visit equal to Week 48 (i.e. the slotted value and the value at

original nominal week 48 visit). The original nominal value will be selected for summary per the rule below for multiple records.

Table 14 Planned Nominal Visit of Health Outcome Data at Maintenance phase

Endpoints	Day1	WK4B	WK5	WK8	WK24	Wk40	WK41	WK44	WK48	WK52
PIN (Q4W)			X				x		x	
HATQoL	x				x				X	
SF-12	x				x				x	
HIVTSQs	x	X			X			x		
HIVTSQc									x	
ACCEPT	x			x	x				x	
NRS (Q4W)		X	x			X	x			
Treatment preference									x	
Willing to switch	X (Q4W)									x (CAR)

13.3.4.3. Evaluable Criteria for Observed Case Displays – PIN and NRS only

Post the visit slotting as described above, data that is assessed outside of 5-9 days post injection at Week 5/41 for NRS/PIN, and data at Week 4b/40 for NRS that is not assessed on the same day as CAB+RPV injections are received will be excluded from Observed Case Displays (see Table 14). However, these data will still be used for LOCF Displays.

Table 15 Evaluable Criteria using Time Window for non-LOCF summaries

Endpoints	WK4B	WK5	Wk40	WK41
PIN (Q4W)		X (within Day 5-9 post injection)		X (within Day 5-9 post injection)
NRS (Q4W)	X (on the same day of WK4B injection)	X (within Day 5-9 post injection)	X (on the same day of WK4B injection)	X (within Day 5-9 post injection)

13.3.5. Assessment Window for PK concentration Data

For PK concentration data at the withdrawal/unscheduled/LTFU Month1visits during Maintenance or Extension phase, the visit will be slotting to the analysis visit per the following steps:

- Identify the 'last nominal visit' with the PK pre-dose assessment performed prior to the visit to be slotted during the same study phase
- The unscheduled/withdrawal/LTFU Month1 visit will be slotted to the nominal visit corresponding to the earliest of the next planned injection visit or next planned PK assessment visit (excluding timepoints with storage PK collection), that is subsequent to the 'last nominal visit' during the same study phase.

During Maintenance or Extension phase, the planned nominal visits for PK Pre-dose are Week 4b, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 96 for Q4W arm; and are Week 56b, 60 for Current ART arm.

For example, if a subject has the 'last nominal visit' (with PK pre-dose assessment) at Week 24 and then withdraws (around Week 28) with a PK assessment labelled at 'LTFU month1' post Week 24 during the Maintenance phase, this assessment will be slotted to the subsequent planned nominal visit of Week 28.

There will be no slotting for planned nominal visits (i.e. analysis visit =visit).

13.3.6. Multiple assessments within an Analysis Window

If after window assignment there are multiple valid assessments of a parameter within the same window, then the following hierarchy will be used to determine the value to be used for summary statistics of observed values:

For data other than health outcome/PK concentration

1. the assessment closest to the window target Study Day;
2. 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.

For Health outcome (excluding NRS) and PK concentration data,

1. If there are multiple assessments assigned to the same analysis visit, the assessment from the planned nominal visit will be used for summary statistics.

For NRS questionnaire assessments:

1. the assessment closest to the window target date will be used;

2. if there are multiple assessments equidistant from the target date, then the earliest assessment will be used.

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 algorithm or LOCF)

13.4. Appendix 4: Study Phases and Treatment State

13.4.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to the Treatment Start Date defined in Section 13.6.1.

AEs will be assigned to study phases as defined in Table 16. For example, adverse events prior to start of Extension phase IP/LTFU ART will be assigned to the Maintenance Phase.

Laboratory data (efficacy, safety, and virology), HIV associated Conditions, health outcomes assessments, vital signs, and ECGs will be assigned to study phases as defined as in Table 17. For example, assessments/events occurring up to and including start of extension phase IP/LTFU ART will be assigned to the Maintenance Phase.

Assessments/events are assigned to study phases sequentially, starting from the top of each table.

Table 16 Assignment of Study Phases for AEs

Study Phase	Date range
Screen	Date < Maintenance Treatment Start Date
Maintenance	**Current ART Arm:** **For subjects continuing into Extension Phase:** Maintenance Treatment Start Date ≤ Date ≤ Start Date of Extension Phase with Oral lead-in of CAB + RPV (expected to be WK52) -1 **For subjects not continuing into Extension Phase:** Date ≥Maintenance Treatment Start Date
	Q4W IM Arm: **For subjects continuing into Extension Phase:** Maintenance Treatment Start Date ≤ **Date** ≤ date of Nominal Week 52 Visit–1 (i.e. the day before Nominal Week 52 Visit). **For subjects not continuing into Extension Phase:** Maintenance Treatment Start Date ≤ **Date** ≤ LTFU ART Start Date -1
Extension	**Subjects Switching from Maintenance Control Arm to Q4W:** Start Date of Extension Phase Oral lead-in of CAB + RPV ≤ **Date** ≤ LTFU ART Start Date -1 **Subjects continuing maintenance Q4W into Extension phase** Date of Nominal Week 52 Visit ≤ **Date** ≤ LTFU ART Start Date -1

- **Date** = AE Start date
- **Maintenance Treatment Start Date:** refer to Treatment Start Date in Section 13.6.1

Table 17 Assignment of Study Phases for Lab assessments (including PK), ECG, Vital Sign, and HIV associated conditions

Study Period	Date range
Screen	Date ≤ Maintenance Treatment Start Date
Maintenance	**Current ART Arm:** **For subjects continuing into Extension Phase:** Maintenance Treatment Start Date < Date ≤ Start Date of Extension Phase Oral lead in of CAB + RPV (expected to be nominal Week 52) **For subjects <u>not</u> continuing into Extension Phase:** Date >Maintenance Treatment Start Date
	Q4W IM Arm: **For subjects continuing into Extension Phase:** Maintenance Treatment Start Date < **Date** ≤ Date of Nominal Week 52 visit **For subjects <u>not</u> continuing into Extension Phase:** Maintenance Treatment Start Date < **Date** ≤ LTFU ART Start Date
Extension	**Subjects Switching from Maintenance Current ART Arm to Q4W IM:** Start Date of Extension Phase Oral lead-in of CAB + RPV < **Date** ≤ LTFU ART Start Date **Subjects continuing maintenance Q4W IM into Extension phase** Date of Nominal Week 52 Injection < **Date** ≤ LTFU ART Start Date

- **Date** = start or assessment date
- **Maintenance Treatment Start Date:** refer to Treatment Start Date in Section 13.6.1

Table 18 Assignment of Study Phases for Concomitant medication/ART

Concomitant during:	Date range
Maintenance	**Current ART Arm:** Maintenance Treatment Start Date ≤ **Medication Taken** < Start Date of Extension Phase Oral CAB + RPV (expected to be Nominal Week 52) or Withdrawn date prior to Extension Phase
	Q4W IM Arms: **For subjects <u>not</u> continuing into Extension Phase:** Maintenance Treatment Start Date ≤ **Medication Taken** < LTFU ART Start Date **For subjects continuing into Extension Phase:** Maintenance Treatment Start Date ≤ **Medication Taken** < Date of Nominal Week 52 visit
Extension	Date of nominal Week 52 visit ≤ **Medication Taken** < LTFU ART Start Date

Note: ART stopped on or before the Maintenance Treatment start date will not be assigned to the Maintenance Phase; ART stopped on or before the date of nominal Week 52 visit will not be assigned to Extension phase.

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

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

Table 19 Assignment to Long-Term Follow-Up Phase

Study Phase	Date range
Long-Term Follow-Up	Date > max(Last IM Injection Date, Last Oral Bridging End Date)

- **Date** = Assessment/Start Date

Note that the long-term follow-up phase and maintenance/extension phases are not necessarily mutually exclusive and are to be defined with separate phase variables in the datasets. For example, an Q4W IM subject who has Week 44 injection and withdrawal at Week 48 without receiving Week 48 injection, the "Week 48 withdrawal visit" belongs to both the maintenance phase and long-term follow-up phase.

In addition to the phases (i.e. Maintenance, Extension, Long term follow up) defined as above, some summaries for AE and LAB data in Q4W IM arm will also be produced for the **'oral lead-in'** period. The 'oral lead-in' period will be defined in separate variables for Q4W IM arm only at maintenance phase, as below:

For AE:

For subjects receiving at least one Maintenance Phase Injection:
Maintenance Treatment Start Date ≤ **Date** < Date of First IM injection
For subjects withdrawing prior to first Maintenance Phase Injection:
Date ≥ Maintenance Treatment Start Date

For non-AE:

For subjects receiving at least one Maintenance Phase Injection:
Maintenance Treatment Start Date < **Date** ≤ Date of First IM injection
For subjects withdrawing prior to first Maintenance Phase Injection:
Date >Maintenance Treatment Start Date

13.4.2. Treatment State

Within each treatment study phase (i.e. Maintenance and Extension—based on assignment of study phase described in Section 13.4.1), only those assessments which occur within the ranges shown in Table 20 will be considered 'on-treatment' for the given phase.

Table 20 Treatment State within Study Phases

Study Phase	Treatment State	Date Range
Screen	Pre-treatment	All assessments/events within phase
Maintenance	On-treatment	Current ART arm: Date ≤ Maintenance Current ART Stop Date + 1
		IM Q4W arm: Date ≤ max(Date of Last Q4W IM Dose + 35, Last Oral dose Date + 1;
	Post-treatment	Current ART arm: Date > Current ART Stop Date + 1
		IM Q4W arm: Date > max(Date of Last Q4W IM Dose + 35, Last Oral dose Date + 1)
Extension	On-treatment	Date ≤ max(Date of Last Q4W IM Dose + 35, Last Oral dose Date + 1)
	Post-treatment	Date > Date of Last Q4W IM Dose + 35, Last Oral dose Date + 1)
Long-Term Follow-up	On-treatment	Date ≤ min(LTFU ART start date, max(Last Injection Date + 35, Last Oral dose Date + 1))
	Post-treatment	Date > min(LTFU ART start date, max(Last Injection Date + 35, Last Oral dose Date + 1))

Note1: Treatment State is determined after data has been assigned to the study phases as defined in Section 13.4.1
Note2: Last Q4W IM / last oral dose/ Maintenance Current ART Stop Date is only applied to subjects who permanently discontinue from study treatment
Note3: Date = Assessment/Start Date.

13.4.2.1. Treatment States for AE Data

For adverse events, partial AE start date will use imputation as described in Section 13.7.2.1. In the case of a completely missing start date, the event will be considered to have started On-treatment at Maintenance phase unless an end date for the AE is provided which is before start of study treatment at Maintenance phase; in such a case the AE is assigned as Pre-treatment.

Within each treatment study phase, only those AE with onset date within the ranges shown in Table 20 will be considered 'on-treatment' for the given phase. The onset date will be derived Based on Table 18.

Table 21 AE onset date, AE duration and relation to study treatment

	Definition
Onset date/study day Since 1st Dose of each study phase (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:

- Onset date/study day will be derived for each study phase, respectively (refer to Section 13.6.1)

13.4.3. Combining Treatment Phases and States

On-treatment and Post-treatment assessments and events will be classified as occurring during the Maintenance Phase, Extension, or Long-term follow up phase.

13.5. Appendix 5: Data Display Standards & Handling Conventions

13.5.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: uk1salx00259
HARP Area	: \ARPROD\GSK1265744\mid201585\week48 : \ARPROD\GSK1265744\mid201585\idmc_01
QC Spreadsheet	: \ARWORK\GSK1265744\mid201585\documents\qc\TBD
Analysis Datasets	
• Analysis datasets for Week 48, 96 will be created according to CDISC standards (SDTM IG Version 3.1.3 & 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 every reporting effort described in the RAP.	

13.5.2. Reporting Standards

General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated (IDSL Standards Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics

Formats
• 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, unless otherwise stated. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the 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:
  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.
• Reporting for Data Listings:
  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1).
  • Unscheduled or unplanned readings will be presented within the subject's listings.

Unscheduled Visits	
• Unscheduled visits will be assigned to a study visit using the all-inclusive windows defined in Section 13.3.2. • However, data summaries will only report visits that are planned assessment time points for each parameter (according to the Time and Events table). • Assessments at unscheduled visits will be included for 'any time On-treatment' time points and in data listings, as well any algorithms that make use of additional data (e.g., Snapshot).	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

13.5.3. Reporting Standards for Pharmacokinetic

Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL Statistical Principle 6.06.1 Assign zero to NQ values (Refer to GUI_51487 for further details)
Reporting of Pharmacokinetic Parameters	
Descriptive Summary Statistics (Log Transformed)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and between geometric coefficient of variation (CVb (%)) will be reported. ○ CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of log transformed data)

13.6. Appendix 6: Derived and Transformed Data

13.6.1. General

Multiple Measurements at One Time Point
• If after window assignment there are multiple valid assessments of a parameter within the same window, then the following hierarchy will be used to determine the value to be used for summary statistics of observed values: o the assessment closest to the window target Study Day; o if there are multiple assessments equidistant from the target Study Day, then for continuous variables the mean of these values will be used and for categorical variables the worse assessment. For HIV-1 RNA, the geometric mean of the number of copies will be used as opposed to the arithmetic mean • Assessments not chosen for use in summary statistics by this algorithm will still appear in the associated listings. Also, such valid assessments will be used when determining values of potential clinical concern for the 'any time On-treatment' time point, and for any algorithm that has specific rules for which observation to use (e.g., Snapshot).

Treatment Start Date

Treatment start date is defined as follows:

Maintenance Phase

- For subjects randomised to Q4W IM, treatment start date is the date of oral lead-in of CAB+RPV entered onto the IP exposure CRF form when study treatment started.
- For subjects randomised to Current ART, treatment start date is the date of the Day 1 visit.

Extension Phase

- For subjects randomised to Q4W IM, treatment start date is the date of Nominal Week 52 injection date.
- For subjects randomised to Current ART, treatment start date is the start date of oral lead-in of CAB+RPV at Extension phase.

Study Day

The Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the start date of study treatment on Maintenance phase as follows:

if date of event ≥ start date of study treatment, then

- $\text{Study Day} = \text{date of event} - \text{start date of treatment on Maintenance phase} + 1$

if date of event < start date of study treatment, then

- $\text{Study Day} = \text{date of event} - \text{start date of treatment on Maintenance phase}$

Note that the start date of study treatment on Maintenance phase 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.

Extension Phase Study Day

The Extension Phase Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the initial start date of Extension phase IP as follows:

if date of event ≥ start date of extension phase IP, then

$$\text{Extension Phase Study Day} = \text{date of event} - \text{start date of Extension phase IP} + 1$$

if date of event < start date of Extension Phase IP, then

$$\text{Extension Phase Study Day} = \text{date of event} - \text{start date of Extension phase IP}$$

Note that the start date of Extension phase IP is considered to be on Extension Phase Study Day 1 and the day before this is Extension Phase Study Day -1; i.e., there is no Extension Phase Study Day 0.

Long-Term Follow Up Study Day
The Long-Term Follow Up (LTFU) Study Day of an event (e.g., lab assessment, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the end of IP treatment [i.e. max(Last IM Injection Date, Last Oral Bridging End Date)] as follows: If the onset of event falls in Long-term Follow up phase, then • LTFU Study Day = date of event - end date of IP
Post-baseline
• Post-baseline refers to the combined time phases of On-treatment and Post-treatment. Post-baseline may be further specified according to phase(s) of the study: Maintenance and Extension (for example, post-baseline across the maintenance and extension phases combined).
Study treatment/drugs
• Refers to either investigation product (CAB+RPV oral /CAB+ RPV LA) or Current ARTs

13.6.2. 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 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. Subjects positive for HBV are not allowed to enter the study.
Lipid-modifying Agents
• The following ATC codes correspond to lipid-modifying agents:

Demographics

- ATC Level 2: C10
- ATC Level 3: C10A, C10B (if Level 2 is not available)
- ATC Level 4: C10AA, C10AB, C10AC, C10AD, C10AX, C10BA, C10BX (if level 2, 3 are not available)

- Subjects are considered to have used a lipid-modifying agent at baseline if they are taking the medication at the time of their baseline lipid testing date.

Subjects are also considered to have used a lipid-modifying agent at baseline if they stopped their lipid modifying medication within 12 weeks prior to their baseline lipid testing date.

Torsade des Pointes (TdP)

TdP cases will be identified based on Standardised MedDRA Query (SMQ) for Torsade de pointes/QT prolongation, broad (MedDRA). The terms per this reference are listed below.

AE preferred term
Electrocardiogram QT interval abnormal
Electrocardiogram QT prolonged
Long QT syndrome
Long QT syndrome congenital
Torsade de pointes
Ventricular tachycardia
Cardiac arrest
Cardiac death
Cardiac fibrillation
Cardio-respiratory arrest
Electrocardiogram repolarisation abnormality
Electrocardiogram U wave inversion
Electrocardiogram U wave present
Electrocardiogram U-wave abnormality
Loss of consciousness
Sudden cardiac death
Sudden death
Syncope
Ventricular arrhythmia
Ventricular fibrillation
Ventricular flutter
Ventricular tachyarrhythmia

Demographics

Framingham Risk Equation

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

for females:

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

for males:

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

where

$S_0(t) = \{0.9501\text{-females}, \quad 0.88936\text{-males}\}$

TC = total serum cholesterol (mg/dL),
HDL = serum HDL cholesterol (mg/dL),
SBPu = systolic blood pressure (mmHg) if subject is not treated for high blood pressure (note that if a subject is treated for high blood pressure then log(SBPu) = 0)
SBPt = systolic blood pressure (mmHg) if subject is treated for high blood pressure (note that if a subject is not treated for high blood pressure then log(SBPt) = 0)

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

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

- A subject will be considered as treated for high blood pressure if during screening it has specified that is suffering from hypertension.
- 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.
- 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

- Exposure to CAB+RPV (oral lead-in) and CAB LA+RPV LA will be calculated from the IP eCRF pages. Exposure to Current ART will be calculated from the CONART eCRF pages.

Q4W IM arm:

- For Maintenance Phase:
    - Exposure to CAB + RPV (oral lead-in) = IP (oral lead-in) stop date- IP (oral lead-in) start date +1
    - Exposure to CAB LA + RPV LA = Number of IP injections received during Maintenance Phase
    - Overall exposure to IP = min [Date of nominal Week 52 visit, max(Date of last IP injection +35, date of last oral CAB/RPV)] - Oral lead-in CAB/RPV Start Date +1
- For Maintenance + Extension Phase
    - Exposure to CAB LA + RPV LA = Number of IP injections received during Maintenance Phase + Extension Phase
    - Overall Exposure to IP = (Date of last IP injection +35, - Oral CAB/RPV Start Date +1

Current ART arm

- For Maintenance Phase:
    - If a subject continues to Extension phase
      Exposure = (IP Start Date at extension phase – 1) – Day 1 DOV + 1
    - If a subject discontinues prior to Nominal Week 52,
      Exposure = Min (Current ART stop date, withdrawal date) – Day 1 DOV + 1
    - If a subject chooses to complete the study participation at Nominal Week 52 and not to continue to Extension phase, then
      Exposure=completion date – Day 1 DOV +1

Current ART stop date is the last permanently stop date among all ARTs taken during Maintenance phase.

- For Extension Phase (Extension Switch Population only):
    - Exposure to CAB + RPV (oral lead-in) = IP (oral lead-in) stop date- IP (oral lead-in) start date +1
    - Exposure to CAB LA+ RPV LA = Number of IP injections received during Extension Phase
    - Overall exposure to IP = max(Date of last IP injection+35, date of last oral CAP/RPV) - Oral CAB/RPV lead-in Start Date +1
- Duration of dosing in subject years will be calculated as the sum of subject duration of dosing in days (across all subjects)/365.25
- Subjects who were randomised to CAB LA+RPV LA but did not report a IP start date will be categorised as having zero days of exposure.
- Subjects who were randomised to Current ART but withdrew on Day1 will be categorised as having zero days of exposure.
- For Current ART arm, missing IP discontinuation 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.

Adherence to CAB/RPV Injection Schedule

Timeliness of Injections Relative to Date of Projected Dosing Visits are assessed by using "actual injection visit date - projected visit date from Week 4B". Each injection visit is counted only once. Individual CAB and RPV injections administered at the same visit are not counted twice. "Extra" unscheduled injections are excluded from all derivations. For example, if during a scheduled visit a subject receives 1 ml of injection instead of 2 ml due to a dosing error, but returns one week later for the remaining 1 ml injection, then the additional visit is excluded. If a subject receives an extra injection at an unscheduled visit by mistake, this visit will also be excluded.

The categories of Timeliness of Injections Relative to Date of Projected Dosing Visits for summary are listed below:

< -14 days
-14 to - 8 days
-7 to - 4 days
-3 to -2 days -1
0 day
1
2 to 3 days
4 to 7 days
8 to 14 days
>14 days
Missed Injection without Oral Bridging
Missed Injection with Oral Bridging

Corrected QTC

When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fridericia's (QTcF) formulas will be calculated, in msec, depending on the availability of other measurements.

If RR interval (in msec) is provided then missing QTcB and/or QTcF will be derived as

$$QTcB = \frac{QT}{\sqrt{RR/1000}} \qquad QTcF = \frac{QT}{\sqrt[3]{RR/1000}}$$

where uncorrected QT interval is also measured in msec.

If RR interval is not provided directly and one of QTcB or QTcF has been entered, then RR interval can be obtained from the above formulas and used to calculate the other correction method value; i.e.,

$$QTcB = \sqrt{\frac{QTcF^3}{QT}} \qquad QTcF = \sqrt[3]{QT \cdot QTcB^2}$$

13.6.3. Safety

Adverse Events– DAIDS Grading

- Clinical adverse events will be graded based on the Division of AIDS Table for Grading the Severity of Adult and Paediatric Adverse Events Version 2.0, November 2014, as specified in the protocol Appendix 12.2.

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. If a character value starting with "<=x", then the numeric value will be x.
  - Example 1: 2 Significant Digits = '< x ' becomes x – 0.01
  - Example 2: 1 Significant Digit = '> x' or '>=x' becomes x + 0.1
  - Example 3: 0 Significant Digits = '< x' becomes x – 1

Estimate of Glomerular Filtration Rate (GFR)

- Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [Levey, 2012] will be used by the central laboratory to provide an estimate of GFR, in mL/min per 1.73 m2, as follows:

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

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

- The CKD-EPI GFR will also be calculated using Cystatin C, as follows

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

Where Scys is serum cystatin C mg/Liter, min indicates the minimum of Scr/0.8 or 1, and max indicates the maximum of Scys/0.8 or 1

- **Lab Toxicities – DAIDS Grading based on Version 2.0, November 2014, as specified in the protocol of Appendix 12.2**

- Toxicities will be based on the Division of AIDS (DAIDS) grading system, Version 2.0, November 2014, as specified in the protocol of Appendix 12.2. Toxicity grades provided by the central laboratory do not distinguish between abnormally high or low criteria, when both are relevant for a particular parameter.

Laboratory Parameters

- 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 for those ≥Grade 1	Above Midpoint for those ≥Grade 1
Fasted glucose	Hypoglycaemia	Hyperglycaemia
Sodium	Hyponatremia	Hypernatremia
Potassium	Hypokalaemia	Hyperkalaemia

National Cholesterol Education Program (NCEP) Lipid Categories

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

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

Total Cholesterol / HDL Cholesterol Ratio

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

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

Percentage change for lipids

The percentage change from baseline is calculated as:

$$\% \text{ change from baseline} = \frac{\text{value at Week 48} - \text{baseline value}}{\text{baseline value}} \times 100\%$$

Other Safety Endpoints
Columbia Suicide Severity Rating Scale (C-SSRS) (Posner, 2007)
• Missing data will not have any imputation performed (Nilsson, 2013)

13.6.4. Efficacy

Snapshot

• The Snapshot algorithm is intended to be primarily a virologic assessment of the endpoint, and as such follows a "virology first" hierarchy.
• 'HIV-1 RNA <50 c/mL' or 'HIV-1 RNA ≥50 c/mL' within an analysis window (see Table 11) is typically determined by the last available HIV-1 RNA measurement in that window while the subject is On-treatment in the Maintenance Phase (as assigned based on Table 20).
  • When no HIV-1 RNA data is available within a window, a subject cannot be assigned to the category of 'HIV-1 RNA < 50 c/mL'. Depending on the reason for lack of data, the subject will be classified as a 'HIV-1 RNA≥50' 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 'HIV-1 RNA≥50'.
• For each scheduled assessment time, the Snapshot response rate for a given threshold (e.g., <50 c/mL) is defined as:
$\text{Snapshot Response Rate} = \frac{\text{Number of responders in that analysis window}}{\text{Number of subjects in the analysis population}}$
  • For each scheduled assessment time, the Snapshot 'HIV-1 RNA≥50'rate for a given threshold (e.g., ≥50 c/mL) is defined as:
$\text{Snapshot VF Rate} = \frac{\text{Number of VFs in that analysis window}}{\text{Number of subjects in the analysis population}}$
• Full details of the algorithm, including the handling of special cases, are included in Section 13.11

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.
Target Detected / Target Non-Detected/Super low viral load testing
• When a measurement of plasma HIV-1 RNA is below the limit of quantification (i.e. 40 c/mL) and is qualitatively observable that will be denoted as a "Target Detected" measure, while HIV-1 RNA below the limit of quantification that is not qualitatively observable that will be denoted as "Target Not Detected". Any measurements <40 c/mL characterised as "Target Non-Detected" or

"Target Detected" will be captured in the database.

- Super low viral load will also be tested by BioMNTR lab for Viral loads below the limit of quantification at some visits (e.g. Week 48)

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

- The analysis of time to confirmed virologic failure (CVF) or discontinuation due to treatment related reasons (i.e., drug-related AE, intolerability of injections, protocol defined safety stopping criteria, or lack of efficacy) will censor subjects who have not met CVF 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 CVF 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.
- Proportion of Participants without virologic (ERDF) or tolerability (TRDF) failure will be estimated using the Kaplan-Meier nonparametric method based on the time to ERDF or TRDF. The estimated proportion 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 estimate of the standard error used to derive confidence intervals will be based on Greenwood's formula [Kalbfleisch,1980].

Observed Case Summary for Subjects per Viral Load Category by Visit (Maintenance Phase)

- For each visit with scheduled viral load collection (per time and events schedule in the protocol), the Observed Case proportion is defined using available data, with no imputation for missing values.
- Denominator: Number of subjects with on-treatment viral load within the analysis Snapshot visit window (e.g. Week 48 ±6 weeks).
- Numerator: Number of subjects with HIV-1 RNA <threshold (e.g. 50 c/mL) based on the last viral load assessment collected within the analysis Snapshot window (e.g. Week 48 ±6 weeks). For Baseline, the last viral load collected prior to or equal to the date of first maintenance phase study treatment dose will be selected for determining the observed case proportion at this timepoint.

Confirmed Virologic Failure (CVF)

- The definition of CVF is provided in the Protocol, Section 5.4.4 – Definition of Virologic Failure

HIV-1 Disease progression Stage

- Categories:
  - CDC Stage I at baseline to CDC Stage III;
  - CDC Stage II at baseline to CDC Stage III;
  - CDC Stage III at baseline to new CDC Stage III event and
  - CDC Stage I, II, III at baseline to death.

Please refer to Protocol (Appendix 4: CDC Classification for HIV-1 Infection) for defining Stage.

For the purpose of analysis, the CDC at baseline and at post-baseline during maintenance phase will be derived as below:

- At Baseline, the 'Baseline CDC stage' for each subject was assessed by investigator and recorded in the eCRF. However, for the analysis, the Baseline CDC stage will be re-derived based on Baseline CD4+ values as well as whether any HIV-associated conditions present at baseline per the Criteria's thresholds (Appendix 4 in Protocol).
- To analyse disease progression, the most advanced post-baseline CDC stage will be

derived based on the occurrences of new AIDS-defining conditions (please refer to Appendix 4 in Protocol for the list of AIDs-defining Conditions) as well as the nadir value of post-baseline CD4+. For example,

- If a subject with CDC 'Stage I' at baseline had the lowest post-baseline $CD4^+$ =120 cell/mm^3 without new AIDs-defining conditions, then HIV disease progression for this subject would be considered as 'CDC stage I at baseline to CDC stage III'.
- If a subject with CDC 'Stage II' at baseline had the lowest post-baseline $CD4^+$ =220 cell/mm^3 AND had at least one new AIDs-defining condition, then HIV disease progression for this subject would be considered as 'CDC stage II at baseline to CDC stage III'.

Delay in IP Injection

IM dosing is expected to occur every 4 weeks from Week 4b onwards. The Delay in IP injection (days) will be calculated as below:

- Delay in IP injection(days) = Injection date - date of preceding injection – 28 days

Delay in IP injection will be grouped into: ≤1, 2-3, 4-7, >7 days.
The proportion of subjects with HIV-1 RNA≥50 c/mL at Week 48 (Snapshot) will be summarized by last delay in IP Injection. The last delay in IP injection will be the delay in IP injection at Week 48, or the delay in last IP injection prior to Week 48 if a subject does not receive Week 48 injection (i.e. missing visit or withdrawal).

13.6.5. Pharmacokinetic

This document is intended for planning analysis of PK concentration data only. Population pharmacokinetics and identification of important determinants of variability will be described in a separate document.

Plasma CAB and RPV concentration-time data

Plasma samples for determination of CAB and RPV concentration will be collected throughout the Maintenance and Extension Phases of the study. Additional samples will be collected for storage during the Long-Term Follow-Up Phase.
Concentration values below the lower limit of quantification (NQ) will be imputed as zero for summary statistics (R&D Guideline: Non-Compartmental Analysis of Pharmacokinetic Data, GUI_51487 (3.0)) and will be denoted as "NQ" in concentration listings.

Evaluable concentration

PK concentration will be summarized in two ways: 'all data' without regard to timing relative to scheduled time and 'evaluable data'.

The 'evaluable data' are from the samples that met sample collection window criteria. Sampling windows are set relative to the previous dose as follows:

- 1-5 hours for 2-hour post dose samples;
- ± 3-10 days post last injection for 1-week post injection visits;
- ±4 day for pre-dose sample.
- Samples impacted by dosing errors (wrong dose) or oral bridging will also be excluded

Timepoint	Evaluable window	For Programming:
PRE-DOSE: WK4B/56B only	20-28 hrs after last oral dose taken and the last 3 oral doses administered properly	20 hrs ≤ Days Since Last Oral Dose ≤ 28 hrs and the last 3 oral doses administered on the three consecutive days prior to WK4B/56B.
2-HR-POST:	1-5 hrs	1 hrs ≤ Hours Since Last Injection Dose ≤ 5 hrs
1-WK-POST:	3-10 days post last injection	3 d ≤ Days Since Last Dose ≤ 10 d
PRE-DOSE:	±4 days	24 d ≤ Days Since Last Dose ≤ 32d

Relative Time is calculated relative to the date and time of last previous dose. For example, if the time of the last previous dose (e.g. oral lead-in/oral-bridging) is missing, then the relative time for pre-dose PK sample will be set to missing and the sample will not be considered 'evaluable'.

If a pre-dose sample is collected on the same day as the first dose of oral bridging, and the time of the first dose (not recorded in eCRF) is confirmed to be 'after' the collection of pre-dose sample (by medical monitor or Data querying), then this PK sample will not be impacted by the oral bridging.

At Week 4B/56B, the evaluable window and relative time for 2-HR-POST will be derived based on last injection dose (not the last oral dose). The timing of last oral dose will not affect 'evaluable' status with the exception of the last oral dose taken after the 1st injection, i.e. if a subject took the last oral dose after the 1st injection, the 2-HR-POST will not be considered 'evaluable', because of the deviation from the IP administration sequence per protocol.

The time-deviation (hours) from the targeted timepoint will be calculated for the samples of '2-HR-POST' and '1-Week-POST' only using the following formula:

Time_deviation (hrs) for '2-HR-POST' =Sample date.time-last previous injection date.time -2 hours

Time_deviation (hrs) for '1-Week-POST' =Sample date.time-last previous injection date.time -7*24 hours

The following windows are for defining 'evaluable' Long-term Follow-up phase PK concentrations.

TIMEPOINT	EVALUABLE WINDOW	FOR PROGRAMMING:
LTFU MONTH 1	± 4 days	24d ≤ Days Since Last Injection ≤ 32d
LTFU MONTH 3	± 1 Week	77d ≤ Days Since Last Injection ≤ 91d
LTFU MONTH 6	± 2 Week	154d ≤ Days Since Last Injection ≤ 182d
LTFU MONTH 9	± 2 Week	238d ≤ Days Since Last Injection ≤ 266d
LTFU MONTH 12	± 2 Week	322d ≤ Days Since Last Injection ≤ 350d

Pharmacokinetic Parameters

- Population pharmacokinetics and identify important determinants of variability will be described in a separate document.

13.6.6. Health Outcome

HIVTSQs

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

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

HIVTSQc

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

PIN

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

Dimension Score (Chevat, 2008)

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

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

Individual Item Scores

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

SF-12

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

Dimension Score

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

Individual Item Scores

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

HATQoL (Holmes, 1999)

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

Life satisfaction, HIV medications, disclosure worries

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

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

ACCEPT (Acceptance/General Dimension) (Gilet, 2014)

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

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

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

Preference question
Questionnaire with one single dichotomous preference question at Week 48 (Q4W IM arm), Week 96 (Current ART arm).
• Assess the treatment preference: Months injection vs daily oral current ART at Week 48 for 'Q4W IM' arm, and at week 96 for 'Current ART' arm who switched to LA. • Any missing values will remain missing (i.e. no imputation)

13.6.7. Viral Genotype and Phenotype

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

Representation of Amino Acid Changes

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

Resistance Associated Mutations

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

Amino Acids in HIV Integrase for Analysis	H51Y, **T66A/I/K**, **E92Q/V**/G, Q95K, T97A, G118R, **F121Y**, E138A/K/T, G140A/C/R/S**, **Y143C/H/R/K/S/G/A, P145S**, **Q146P**, **S147G**, **Q148H/K/R/N**, **V151**I/**L**/A, S153F/Y, **N155H/**S/T, E157Q, G163R/K, S230R, R263K, L68V/I*, L74I*, E138D*, 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 03Feb2017) and accessed on 07Mar 2017.
- 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 previous DTG study in INI-experienced subjects (ING112574).

  **G140R is potentially associated with CAB based on in-stream data monitoring of CVF subjects

- 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 [Wensing, 2017].

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, 2017]

Genotypic/ Phenotypic/Net Assessment Susceptibility (Plasma sample at time of CVF), Genotypic Susceptibility (PBMC at Baseline)

Phenotypic Susceptibility

Phenotypic susceptibility to all licensed antiretroviral drugs and CAB 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 assay to assay, FC values that are greater than the maximum assay limit (e.g., '>100') will be interpreted as having a value equal to the smallest maximum assay limit for that ART in the study population for data analysis. Censored values will be presented 'as is' in the listings. Phenotypic susceptibilities will be categorised according to FC as shown in Table 8 (based on Monogram PhenoSense assay). Clinical cutoffs (where available) or biological cutoffs by PhenoSense will be used to define the phenotypic susceptibility of background treatment by Monogram.

Replication capacity is generated as part of standard phenotypic assays

PhenoSense Algorithm

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 (TAF)	NRTI	(1.4 – 4) [a]
Delavirdine	DLV	NNRTI	6.2
Efavirenz	EFV	NNRTI	3
Nevirapine	NVP	NNRTI	4.5
Etravirine	ETR	NNRTI	(2.9-10) [a]
Rilpivirine	RPV	NNRTI	2.0
Fosamprenavir/r	FPV/r	PI	(4-11) [a]
Atazanavir/r	ATV/r	PI	5.2 [a]
Indinavir/r	IDV/r	PI	10 [a]
Lopinavir/r	LPV/r	PI	(9 – 55) [a]
Nelfinavir	NFV	PI	3.6
Saquinavir/r	SQV/r	PI	(2.3 – 12) [a]
Tipranavir/r	TPV/r	PI	(2 – 8) [a]
Darunavir/r	DRV/r	PI	(10 – 90) [a]
Ritonavir	RTV	PI	2.5
Enfuvirtide	T20	FI	6.48
Cabotegravir	CAB	INI	2.5
Raltegravir	RAL	INI	1.5
Elvitegravir	EVG	INI	2.5
Dolutegravir	DTG	INI	(4-13) [a]

a. clinical cutoff (lower cutoff – higher cutoff).

Phenotypic susceptibility to each drug in a subject's background regimen is determined by applying drug-associated cutoffs as defined by the PhenoSense algorithm to the phenotypic fold resistance as below:

Full Sensitivity

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

Partial Sensitivity

Fold Change	Interpretation
> clinical higher cutoff	resistance
≤ clinical higher cutoff and > clinical lower cutoff	partially sensitive
≤ clinical lower cutoff	sensitive

PHENOTYP dataset from Monogram contains the phenotypic susceptibility for each drug derived from the cutoff listed above. Thus, phenotypic susceptibility (i.e. full sensitivity and partial sensitivity) will not be re-derived for our analysis.

Genotypic and Net Assessment Susceptibility

Genotypic and Net assessment susceptibility to all licensed antiretroviral drugs and CAB will be determined from Monogram Inc. and will be reported with the categories of 'resistance', 'partially sensitive', and 'sensitive' as what will be performed for phenotypic susceptibility. Genotypic and Net assessment susceptibility will be assessed at time of CVF using plasma sample, Genotypic susceptibility will be assessed at baseline using PBMC.

13.7. Appendix 7: Reporting Standards for Missing Data

13.7.1. Premature Withdrawals

Element	Reporting Detail

General	• Subject study completion (i.e. as specified in the protocol) was defined as:
	  ○ Randomly assigned to either treatment group, completed the randomized Maintenance Phase including the Nominal Week 52 visit, and did not enter the Extension Phase;
	  ○ Randomly assigned to either treatment group, completed the randomized Maintenance Phase including the Nominal Week 52 visit, and entered and completed the Extension Phase (defined as remaining on study until transitioning to ATLAS-2M, or commercial supplies of CAB LA + RPV LA become locally available, or development of CAB LA + RPV LA is terminated).
	Participants who withdraw from CAB LA + RPV LA and go into the Long-Term Follow Up Phase will be considered to have prematurely withdrawn from the study, even if they complete the 52-week follow-up phase. In addition to the 52 week Long-Term Follow-Up Phase required for participants randomized to CAB LA + RPV LA, an in-clinic Follow-Up visit will be conducted approximately 4 weeks after the last dose of study medication for participants randomized to the Current ART arm with ongoing AEs, SAEs, and also any laboratory abnormalities that are considered to be AEs or potentially harmful to the participant, at the last on-study visit. Assessments at the Follow-up visit should reflect any ongoing complaints (e.g., blood draws to follow a laboratory abnormality). Follow-Up visits are not required for successful completion of the study.
	• Withdrawn subjects were not replaced in the study.
	• All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.
	• Withdrawal visits will be slotted as per Appendix 3: Assessment Windows or will be summarised as withdrawal visits.

13.7.2. 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:
	  ○ These data will be indicated by the use of a “blank” in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table.
	  ○ Answers such as “Not applicable” and “Not evaluable” are not considered to be missing data and should be displayed as such.

Outliers	• Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

13.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start date; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: ○ Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 4: Study Phases and Treatment State ○ Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.
Concomitant Medications/ Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month ○ 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 Screening date will be used. • The recorded partial date will be displayed in listings.
Health outcomes	• For the health outcomes questionnaire data, please refer to Section 13.6.6. • For the summary of individual item scores outputs, missing scores will not be computed.

13.7.2.2. 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) do not belong to 'HIV-1 RNA < 50 c/mL (or <200 c/mL)'. The nature of this missing data will be further classified in Snapshot summaries as either 'HIV-1 RNA≥50' or 'No Virologic Data at Week X'; Appendix 11: Snapshot Algorithm Details for full details
LOCF	• In the LOCF dataset, missing values will be carried forward from the previous, non-missing available on-treatment assessment. If the baseline value is missing any missing values until the first non-missing value will remain missing.
Lipid LOCF	**Baseline for Lipids LOCF Analyses**: ● Last evaluable lipids assessment up to and including the start of IP, where 'evaluable' is defined as: Lipid modifying agents not taken within 12 weeks of the date of assessment and Lipids are collected in a fasting state. **Subjects with unevaluable Baseline for Lipids (as defined above) will be excluded from this dataset.**

Element	Reporting Detail
	Post-Baseline: ● 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 at visits with observed on-treatment values will continue even if the subject discontinues the lipid-lowering agent. Missing assessments will not be imputed **Analyses Evaluated with Lipid LOCF dataset:** This dataset will be used to summarize fasting lipids parameters in the following displays: ● Summary of Chemistry Values by visit ● Summary of Chemistry Change from Baseline by visit ● Summary of TC/HDL ratio Change from Baseline. • All other displays of lipids (i.e. toxicity tables and NCEP tables) will use observed fasting data, without LOCF imputation

13.8. Appendix 8: Values of Potential Clinical Importance

Element	Reporting Detail
Laboratory Values and Adverse Events	• The central laboratory will flag lab parameter toxicities directly in the provided datasets based on Division of AIDS Table for Grading the Severity of Adult and Paediatric Adverse Events Version 2.0, November 2014

13.9. Appendix 9: Population Pharmacokinetic (PopPK) Analyses

PopPK will be described in a separate document.

13.10. Appendix 10: Pharmacokinetic / Pharmacodynamic Analyses

PK/PD dataset specification and methodology will be described in a separate document.

13.11. Appendix 11: Snapshot Algorithm Details

Detailed Algorithm Steps

- Consider an analysis visit window for Week X (e.g. Week4, …Week 24, Week 48 et al). The Window for Week 24/48 visit is defined in Table 11 (e.g. window for Week 48 is ± 6 Week: 295 ≤ Study Day ≤ 378) and in Table 9 for other visits through to Nominal Week 52 at Maintenance Phase. The Snapshot Analysis at post Maintenance Phase will not be appropriate because a large portion of responders will be switched to other studies and not all subjects would have the chance to reach same timepoint.
- The HIV1-RNA threshold of 50, 200 copies/mL will be analysed, respectively, in this study
- The analysis window 'Week 48' and HIV1-RNA threshold of '50 copies/mL' are used for the purpose of illustration. A subject's Snapshot response and reason at Week 48 are categorized as below.
    - HIV1-RNA < 50 copies/mL
    - HIV1-RNA ≥ 50 copies/mL
        - Data in window not below 50
        - Discontinued for lack of efficacy
        - Discontinued for other reason while not below 50
        - Change in background therapy*
    - No Virologic Data at Week 48 Window
        - Discontinued study due to AE or death
        - Discontinued study for other reasons
        - On study but missing data in window

* Note: since changes in ART are not permitted in this protocol, all such subjects who change ART during the maintenance phase will be considered 'HIV1-RNA ≥ 50 copies/mL'. if the change in ART is made prior to an analysis timepoint. Subjects with protocol permitted oral bridging treatment will not be considered ' HIV1-RNA ≥ 50 copies/mL' due to 'change in ART'.

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

Detailed steps

Please note that the following scenarios will NOT be penalized Per Snapshot algorithm (i.e. please excluding these scenarios from **Condition** 1-4).

- Dose reduction, dropping a component, or change in formulation (e.g. 'Tivicay + Kivexa' to 'Triumeq' with the identical ingredients)

Condition ('Week 48' indicates Week 48 window)	**Response**	**Reasons**
1. If ***non-permitted*** change in background therapy ***prior to*** Week 48	HIV1-RNA ≥ 50	Change in background therapy
2.If ***permitted*** change[a] in background therapy ***prior to*** Week 48 AND the latest on-treatment VL prior to/on the date of change is ≥ 50 c/m (NA to this study)	HIV1-RNA ≥ 50	Change in background therapy

Condition ('Week 48' indicates Week 48 window)	**Response**	**Reasons**
3: If ***non-permitted*** change in background therapy ***during*** Week 48		
• Last on-treatment VL during Week 48 prior to/on the date of change ≥ 50 c/mL	HIV1-RNA ≥ 50	Data in window not below 50
• Last on-treatment VL during Week 48 prior to/on the date of change <50 c/mL	HIV1-RNA < 50	
• No VL during Week 48 prior to/on the date of change	HIV1-RNA ≥ 50	Change in background therapy
4: If ***permitted*** change[a] in background therapy ***during*** Week 48 AND the last on-treatment VL prior to/on the date of change is ≥ 50 c/mL (NA to this study)		
4.1 this last on-treatment VL occurs prior to Week 48	HIV1-RNA ≥ 50	Change in background therapy
4. 2 this last on-treatment VL occurs during Week 48 but prior to/on the date of change	HIV1-RNA ≥ 50	Data in window not below 50
5: If none of the above conditions met		
5.1 VL available during Week 48		
• Last on-treatment VL during Week 48 ≥ 50 c/mL	HIV1-RNA ≥ 50	Data in window not below 50
• Last on-treatment VL during Week 48 <50 c/mL	HIV1-RNA < 50	
5.2 No VL during Week 48		
if subjects still on study, i.e. the upper bound of analysis snapshot window is prior/equal to the following date Current ART arm: Min (Current ART Stop Date + 1, withdrawal date) IM Q4W arm: Min[max(Date of last Q4W IM Dose + 35, Date of last oral dose+1), withdrawal date]	No virologic data at Week 48 Window	On study but missing data in window

Condition ('Week 48' indicates Week 48 window)	**Response**	**Reasons**
5.2.1 If subjects withdraw before/during Week 48 due to		
5.2.1.1 Safety reasons (e.g. AE/death, liver chemistry stopping criteria, renal toxicity withdrawal criteria, QTc withdrawal criteria et al, as recorded in eCRF Conclusion form)	No virologic data at Week 48 Window	Disc due to AE/death
5.2.1.2 Non-safety related reasons (e.g. Lack of efficacy, protocol deviation, withdrew consent, loss to follow-up, study closed/terminated, investigator discretion et al, as recorded in eCRF Conclusion Form)		
• Last on-treatment VL <50 c/mL OR no on-treatment VL available during study	No virologic Data at Week 48 Window	Disc for other reasons
• Last on-treatment VL ≥ 50 c/mL AND withdrawal due to Lack of efficacy	HIV1-RNA ≥ 50	Disc. for lack of efficacy
• Last on-treatment VL ≥ 50 c/mL AND withdrawal due to all other non-safety related reasons	HIV1-RNA ≥ 50	Dis. for other reason while not below 50

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

Examples from FDA guidance

Data in Window

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

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

No Data in Window

Discontinued study due to Adverse Event or Death:

- Any patient who discontinues because of an AE or death before the window should be classified as *Discontinued due to AE or Death* (as appropriate), regardless of the HIV-RNA result, even if the HIV-RNA is below 50 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 having HIV-RNA below 50 copies/mL.

b. HIV-RNA is 552 copies/mL on Day 336 and the patient discontinues on Day 360, the patient is categorized as having HIV-RNA greater than or equal to 50 copies/mL.

Discontinued for Other Reasons:

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

On study but missing data in window:

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

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

13.12. Appendix 12: Abbreviations & Trade Marks

13.12.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
BMD	Bone Mineral Density
BMI	Body Mass Index
CAB	Cabotegravir
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CMH	Cochran-Mantel-Haenszel
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSR	Clinical Study Report
C-SSRS	Columbia Suicide Severity Rating Scale
CTR	Clinical Trial Register
CVb	Coefficient of Variation (Between)
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
CVD	Cardiovascular Disease
CVF	Confirmed Virologic Failure
DAIDS	Division of AIDS
DBF	Database Freeze
DBR	Database Release
DOB	Date of Birth
DP	Decimal Place
DTG	Dolutegravir
eCRF	Electronic Case Record Form
eGFR	Estimated Glomerular Filtration Rate
EMA	European Medicines Agency
ERDF	Efficacy Related Discontinuation Failure
ESP	Extension Switch Population
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act
FSFV	First Subject First Visit
GSK	GlaxoSmithKline
GUI	Guidance
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HSR	Hypersensitivity Reaction
IA	Interim Analysis
ICH	International Conference on Harmonisation
IDMC	Independent Data Monitoring Committee

IDSL	Integrated Data Standards Library
IMMS	International Modules Management System
INI	Integrase Inhibitors
IP	Investigational Product
ITT	Intent-To-Treat
ITT-E	Intent-To-Treat Exposed
LOCF	Last Observation Carries Forward
MMRM	Mixed Model Repeated Measures
NCEP	National Cholesterol Education Program
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitors
NQ	Non Quantifiable
NRTI	Nucleoside Reverse Transcriptase Inhibitors
OC	Observed Case
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PI	Protease Inhibitors
PK	Pharmacokinetic
PopPK	Population PK
PP	Per Protocol
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAMOS	Randomisation & Medication Ordering System
RAP	Reporting & Analysis Plan
RPV	Rilpivirine
SAE	Serious Adverse Event
SAC	Statistical Analysis Complete
SD	Standard Deviation
SDAC	Statistics Data Analysis Centre
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
TA	Therapeutic Area
TFL	Tables, Figures & Listings
TRDF	Treatment Related Discontinuation Failure

13.12.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
Dolutegravir
Triumeq

Trademarks not owned by the GlaxoSmithKline Group of Companies
NONMEM
Rilpivirine
SAS
WinNonlin

13.13. Appendix 13: List of Data Displays

13.13.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.01 to 1.n	1.01 to 1.n
Efficacy	2.01 to 2.n	2.01 to 2.n
Safety	3.01 to 3.n	3.01 to 3.n
Pharmacokinetic	4.01 to 4.n	4.01 to 4.n
Pharmacokinetic / Pharmacodynamic	5.01 to 5.n	5.01 to 5.n
Health Outcomes	6.01 to 6.n	6.01 to 6.n
Virology	7.01 to 7.n	7.01 to 7.n
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	y to z	

13.13.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required an example mock-up displays provided a separate document.

13.13.3. Deliverables

Delivery [1]	Description
IDMC_CVF monitoring	Refer to IDMC Charter, Section 12.3, Appendix C
IDMC_Futility at Week 24	Refer to IDMC Charter, Section 12.3, Appendix C
IDMC_Futility adhoc	Refer to file-note IDMC Adhoc Analysis
HL	Headline at Week 48
WK48	Week 48
WK96	Week 96
EOS	End of study

NOTES:

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

13.13.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.1.	All Subjects Screened	SP1	Summary of Study Populations	CS CORE	WK48, 96, EOS
1.2.	All Subjects Screened	Shell TSP1	Summary of Subjects by country and investigator		WK48, 96, EOS
1.3.	All Subjects Screened	ES6	Summary of Screening Status and Reasons for Screening Failures	CS CORE	WK48, 96, EOS
1.4.	ITT-E	EudraCT age	Summary of Age Categories	CS CORE	WK48, 96, EOS
1.5.	ITT-E	ES1	Summary of Subject Accountability: Study Conclusion Record – ITT-E	ICH E3, GSK CTR, FDAAA, EudraCT	WK48, 96, EOS
1.6.	ITT-E	ES1	Summary of CAB+RPV Discontinuation for randomized Q4W Arm	CS CORE	WK48, 96, EOS
1.7.	ITT-E	ES1	Summary of Subject Accountability: Maintenance Phase Conclusion Record – ITT-E	ICH E3, GSK CTR, FDAAA, EudraCT	HL, WK48
1.8.	ESP	ES1	Summary of CAB+RPV Discontinuation for Randomized Current ART Arm during Extension Phase	CS CORE	WK48, 96, EOS

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.9.	LTFU	ES1	Summary of Subject Accountability: Long-term follow up Phase Conclusion Record – LTFU	ICH E3, GSK CTR, FDAAA, EudraCT	WK48, 96, EOS
1.10.	ITT-E	HIV_ES1	Summary of Subject Accountability: Withdrawals by Visit at Maintenance phase		WK48
1.11.	ITT-E	HIV_ES1	Summary of Subject Accountability: Maintenance+extension phase Conclusion Record	For Q4W arm only	WK48, 96, EOS
1.12.	ESP	HIV_ES1	Summary of Subject Accountability: Extension phase Conclusion Record	For Current art arm only	WK48, 96, EOS
1.13.	ITT-E	DV1	Summary of Important Protocol Deviations (Maintenance phase)	CS CORE, At wk96, Maintenance+extension phase for those Q4W IM arm; and Extension phase only for ESP,	WK48
1.14.	ITT-E	SA2	Summary of Protocol Deviations Leading to Exclusion from the Per-Protocol Population (Maintenance phase)	CS CORE	WK48
1.15.	ITT-E	IE1	Summary of Inclusion/Exclusion Criteria Deviations		WK48, 96, EOS
Demography and Baseline					
1.16.	ITT-E	Shell TSP2	Summary of Demographic Characteristics	See also DM1 in IDSL	HL, WK48, 96, EOS
1.17.	ITT-E	DM5	Summary of Race and Racial Combinations	CS CORE	WK48, 96, EOS
1.18.	ITT-E	DM6	Summary of Race and Racial Combinations Details	CS CORE	WK48, 96, EOS
1.19.	ITT-E	Shell TSP3	Summary of Hepatitis Status at Entry		WK48, 96, EOS
1.20.	ITT-E	CDC1	Summary of Derived CDC Stages of HIV Infection at Baseline		WK48, 96, EOS
1.21.	ITT-E	Shell TSP4	Summary of Baseline Cardiovascular Risk Assessments		WK48, 96, EOS
1.22.	ITT-E	Shell TSP5	Distribution of CD4+ Cell Count Results at Screening and Baseline		WK48, 96, EOS

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Medical Conditions, Concomitant Medications & Antiretroviral Therapy					
1.23.	ITT-E	MH1	Summary of Current Medical Conditions	CS CORE	WK48, 96, EOS
1.24.	ITT-E	MH1	Summary of Past Medical Conditions	CS CORE	WK48, 96, EOS
1.25.	ITT-E	MH4	Summary of Current Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, Nervous System Conditions, and Hepatobiliary disorders		WK48, 96, EOS
1.26.	ITT-E	MH4	Summary of Past Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, Nervous System Conditions, and Hepatobiliary disorders		WK48, 96, EOS
1.27.	ITT-E	CM8	Summary of Concomitant Medication Ingredient Combinations (Maintenance phase)	At wk96/EOS, Maintenance+extension phase for those Q4W IM arm; and Extension phase only for ESP ,	WK48, 96, EOS
1.28.	ITT-E	Shell TSP6	Summary of Antiretroviral Therapy stopped prior to Screening		WK48, 96, EOS
1.29.	ITT-E	Shell TSP7	Summary of Antiretroviral Therapy Taken during Screening		WK48, 96, EOS
1.30.	ITT-E	TSP11	Summary of Antiretroviral Regimen Taken during Screening		WK48, 96, EOS
1.31.	ITT-E	Shell TSP7a	Time Since First Antiretroviral Therapy until Maintenance Phase Start		WK48, 96, EOS
1.32.	ITT-E	Shell TSP8	Summary of Baseline third agent class		HL, WK48, 96, EOS
1.33.	ITT-E	Shell TSP9	Summary of Lipid Modifying Agent Use at Baseline		WK48, 96, EOS
1.34.	ITT-E	Shell TSP10	Summary of Lipid Modifying Agent Use Starting Post-Baseline (Maintenance phase))		WK48, 96, EOS
1.35.	ITT-E	SU1	Summary of Substance use		WK48, 96, EOS
1.36.	ITT-E	Shell TSP12	Summary of HIV Risk Factor		WK48 96, EOS

13.13.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Primary Efficacy Analyses					
2.1	ITT-E	Shell TPEF1	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA ≥50 c/mL at Week 48 (Maintenance Phase) – Snapshot Analysis – ITT-E		HL, WK48
2.2	Per-Protocol	Shell TPEF1	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA ≥50 c/mL at Week 48 (Maintenance Phase) – Snapshot Analysis - PP		WK48
2.4	ITT-E	Shell TPEF2	Summary of Study Outcomes (≥50 c/mL) at Week 48(Maintenance Phase) – Snapshot Analysis		HL, WK48
2.5	ITT-E	Shell TPEF3	Treatment by Strata Tests of Homogeneity for Proportion of Subjects with Plasma HIV-1 RNA ≥50 c/mL at Week 48 (Maintenance Phase) - Snapshot Analysis		WK48
2.6	ITT-E	Shell TPEF4	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA ≥50 c/mL at Week 48 by Subgroup (Maintenance Phase) - Snapshot Analysis		WK48
2.7	ITT-E	Shell TPEF5	Summary of Study Outcomes (≥50 c/mL) at Week 48 by Subgroup (Maintenance Phase) – Snapshot Analysis		WK48
Secondary Efficacy Analyses					
2.8	ITT-E	Shell TPEF1	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 (Maintenance Phase) – Snapshot Analysis – ITT-E		HL, WK48
2.9	Per-Protocol	Shell TPEF1	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 (Maintenance Phase) – Snapshot Analysis - PP		HL, WK48
2.10	ITT-E	Shell TPEF3	Treatment by Strata Tests of Homogeneity for Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 (Maintenance Phase) - Snapshot Analysis		WK48

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.11	ITT-E	Shell TPEF4	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 by Subgroup (Maintenance Phase) - Snapshot Analysis		WK48
2.12	ITT-E	Shell TSEF2	Proportion of Subjects with Plasma HIV-1 RNA ≥50 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		WK48
2.13	ITT-E	Shell TSEF2.1	Proportion of Subjects with Plasma HIV-1 RNA ≥50 c/mL by Subgroup and Visit (Maintenance Phase) – Snapshot Analysis		WK48
2.14	ITT-E	Shell TSEF7.0	Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Failure by Week 48 duringMaintenance Phase - *Treatment Related Discontinuation = Failure*		WK48
2.15	ITT-E	Shell TSEF7.1	Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Failure by Week 48 during Maintenance Phase - *Efficacy Related Discontinuation = Failure*		WK48
2.16	ITT-E	Shell TSEF2	Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		WK48
2.17	ITT-E	Shell TSEF2	Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Subgroup and Visit (Maintenance Phase) – Snapshot Analysis		WK48
2.18	ITT-E	Shell TSEF2	Proportion of Subjects with Plasma HIV-1 RNA <200 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		WK48
2.19	ITT-E	Shell TSEF9	Proportion of subjects with HIV-1 RNA≥50 c/mL at Week 48 (Snapshot) by Last Delay in IP Injection (Maintenance Phase)	For Q4W IM arm only. The last delay in IP injection is the delay in IP injection at Week 48, or delay in last IP injection prior to Week 48 if a subject has no injection at WK48 (e.g. missing visit or early withdrawal)	WK48,
2.20	ITT-E	Shell TSEF8	Summary of Plasma HIV-1 RNA by Visit		WK48, 96, EOS

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.21	ITT-E	Shell TSEF3	Proportion of Subjects Meeting Confirmed Virologic Failure Criteria by Visit (Maintenance Phase)		HL, WK48
2.22	ITT-E	Shell TSEF3	Proportion of Subjects Meeting Confirmed Virologic Failure Criteria by Visit for Q4W Arm Only (Maintenance + Extension Phase)		WK96, EOS
2.23	ESP	Shell TSEF3	Proportion of Subjects Meeting Confirmed Virologic Failure Criteria by Visit for Current ART Arm Only (Extension Phase)		WK96. EOS
2.24	CVF	Shell TSEF4	Summary of Plasma HIV-1 RNA Results at Suspected and Confirmation of Confirmed Virologic Failure – Maintenance phase		WK48
2.25	ITT-E	Shell TSEF5	Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) by Visit (Maintenance Phase)		WK48, 96, EOS
2.26	ITT-E	Shell TSEF5	Summary of CD4+ Cell Count (cells/mm^3) by Visit (Maintenance Phase)		WK48, 96, EOS
2.27	ITT-E	Shell TSEF5	Summary of CD8+ Cell Count (cells/mm^3) by Visit (Maintenance Phase)		WK48, 96, EOS
2.28	ITT-E	Shell TSEF5	Summary of Change from Baseline in CD8+ Cell Count (cells/mm^3) by Visit (Maintenance Phase)		WK48, 96, EOS
2.29	ITT-E	Shell TSEF5	Summary of CD4+/CD8+ Ratio Cell Count (cells/mm^3) by Visit	While both CD4+ and CD8+ are available on the same date	WK48, 96, EOS
2.30	ITT-E	HIV1/Shell TSEF 6.0	Summary of Post-Baseline HIV-1 Associated Conditions Including Recurrences (Maintenance Phase)		WK48
2.31	ITT-E	HIV1/Shell TSEF 6.0	Summary of Post-Baseline HIV-1 Associated Conditions Excluding Recurrences (Maintenance Phase)		WK48
2.32	ITT-E	HIV2/Shell TSEF6.1	Summary of Post-Baseline HIV-1 Disease Progressions (Maintenance Phase)		WK48
2.34	ITT-E	Table 7.1026 (Latte2/week48idsl)/ Shell TSEF12	Proportion of Subjects with Plasma HIV-1 RNA <2 copies/mL by Visit - Observed Case Analysis		WK48

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.36	ITT-E	Shell TPEF2	Summary of Study Outcomes (≥200 c/mL) at Week 48 (Maintenance Phase) – Snapshot Analysis		WK48
2.37	ITT-E	Shell TSEF11	Summary of Subjects per Viral Load Category by Visit (Maintenance Phase)		Wk48
2.38	ITT-E	Shell TSEF5	Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) at Week 48 by Subgroup (Maintenance Phase)		WK48

13.13.6. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Primary Efficacy Analyses					
2.1.	ITT - E	Shell FPEF1	Proportion (95% CI) of Subjects with HIV-1 RNA ≥50 c/mL by Visit – Snapshot Analysis		HL, WK48
2.2.	ITT - E	Shell FPEF2	Unadjusted Treatment Difference in Proportion (95% CI) of Subjects with HIV-1 RNA ≥50 c/mL at Week 48 by Subgroup – Snapshot Analysis		WK48
Secondary Efficacy Analyses					
2.3.	ITT - E	Shell FPEF1	Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL by Visit – Snapshot Analysis		HL, WK48
2.4.	ITT - E	Shell FPEF2	Unadjusted Treatment Difference in Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL at Week 48 by Subgroup – Snapshot Analysis		WK48

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.5.	ITT - E	Shell FPEF1	Proportion (95% CI) of Subjects with HIV-1 RNA <200 c/mL by Visit – Snapshot Analysis		WK48
2.6.	ITT-E	Mid200056//wk96cdisc/Figure 7.1007	Individual Plasma HIV-1 RNA (log10 copies/mL) Profiles by Visit – for CVF subjects (for Q4W arm)	The 1st vertical line indicates start of study treatment at Maintenance phase. The second vertical reference line indicates last IP on-treatment study day. i.e. min(last IP injection dose+35 days, LTFT HAART start date, date of last oral CAB+RPV+1). This vertical line is only for subjects who withdraw from Maintenance/Extension phase'	HL, WK48, 96, EOS

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.7.	ITT-E	Mid200056//wk96cdisc/Figure 7.1007	Individual Plasma HIV-1 RNA (log10 copies/mL) Profiles by Visit – for CVF subjects (for Current ART arm)	The 1st vertical line indicates start of study treatment at Maintenance phase. The second vertical reference line indicates last on-treatment study day of Current ART. i.e. date of last Current ART dose; The third vertical reference line indicates last IP on-treatment study day. i.e. min(last IP injection dose+35 days, LTFT HAART start date, date of last oral CAB+RPV+1). The 2nd vertical reference line is only for subjects who withdraw or completed Maintenance phase, the 3rd vertical reference line is only for those withdraw from Extension phase	HL, WK48, 96, EOS
2.8.	ITT - E	Mid200056//wk96cdisc/Figure 7.1007	Individual Plasma HIV-1 RNA for subjects who are in the category of 'viral load ≥50 c/mL' at Week 48 per Snapshot algorithm (for Q4W arm)	The 1st vertical line indicates start of study treatment at Maintenance phase. The second vertical reference line indicates last IP on-treatment study day. i.e. min(last IP injection dose+35 days, LTFT HAART start date, date of last oral CAB+RPV+1). This vertical line is only for subjects who withdraw from Maintenance/Extension phase'	HL, WK48, 96, EOS

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.9.	ITT - E	Mid200056//wk96cdisc/Figure 7.1007	Individual Plasma HIV-1 RNA for subjects who are in the category of 'viral load ≥50 c/mL' at Week 48 per Snapshot algorithm (for Current ART arm)	The 1st vertical line indicates start of study treatment at Maintenance phase. The second vertical reference line indicates last on-treatment study day of Current ART. i.e. date of last Current ART dose; The third vertical reference line indicates last IP on-treatment study day. i.e. min(last IP injection dose+35 days, LTFT HAART start date, date of last oral CAB+RPV+1). The 2nd vertical reference line is only for subjects who withdraw or completed Maintenance phase, the 3rd vertical reference line is only for those withdraw from Extension phase	HL, WK48, 96, EOS
2.10.	ITT - E	Shell FPEF1	Proportion (95% CI) of Subjects with HIV-1 RNA >=200 c/mL by Visit – Snapshot Analysis		WK48

13.13.7. Safety Tables

Safety Tables (Displays will be for both treatment arms, unless specified)					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure					
3.1.	Safety	Shell TS1.1	Summary of Extent of Exposure to Investigational Product – Maintenance Phase	CS Core	WK48, 96, EOS
3.2.	Safety	Shell TS1.1	Summary of Extent of Exposure to Investigational Product – Maintenance Phase + Extension Phase (for Q4W IM arm)	CS Core (only for Q4W arm)	WK48, 96, EOS
3.3.	ESP	Shell TS1.1	Summary of Extent of Exposure to Investigational Product – Extension Phase only	CS Core (only for Current ART)	WK48, 96, EOS
3.4.	Safety	Shell TS1.2	Summary of Needle Length and Gauge for CAB Injection - Maintenance Phase	(only for Q4W arm)	WK48
3.5.	Safety	Shell TS1.2	Summary of Needle Length and Gauge for RPV Injection - Maintenance Phase	(only for Q4W arm)	WK48
3.6.	Safety	Shell TS1.3	Summary of Adherence to Q4W IM Dosing Schedule (Maintenance phase)	(only for Q4W arm) please refer to Section 13.6.2-- Adherence to CAB/RPV Injection Schedule	WK48
Adverse Events					
3.7.	Safety	AE1	Summary of All Adverse Events by System Organ Class – Maintenance Phase	CS Core (optional)	WK48
3.8.	Safety	AE5B	Summary of All Adverse Events by System Organ Class and Maximum Toxicity – Maintenance Phase	CS Core	HL, WK48
3.9.	Safety	AE5B	Summary of All Adverse Events by System Organ Class and Maximum Toxicity – Maintenance + Extension Phase	CS Core ((only for Q4W arm)	WK48, 96, EOS
3.10.	ESP	AE5B	Summary of All Adverse Events by System Organ Class and Maximum Toxicity – Extension Phase	CS Core (only for Current ART)	WK48, 96, EOS

Safety Tables (Displays will be for both treatment arms, unless specified)					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.11.	Safety	AE5B	Summary of All On-treatment Adverse Events by System Organ Class and Maximum Toxicity – Maintenance Phase	CS Core	WK48
3.12.	LTFU	AE5B	Summary of All Adverse Events by System Organ Class and Maximum Toxicity – Long-term Follow-up Phase	CS Core	WK 96, EOS
3.13.	Safety	AE5B	Summary of All Adverse Events by System Organ Class and Maximum Toxicity – Oral Lead-in Period at Maintenance phase	CS Core (for Q4W arm only)	HL, WK48
3.14.	Safety	AE3	Summary of Common Adverse Events (.>=5%) by Overall Frequency – Maintenance Phase	CS Core	WK48
3.15.	Safety	AE3	Summary of Common Grade 2-5 Adverse Events (>=1%) by Overall Frequency – Maintenance Phase		WK48
3.16.	Safety	AE1	Summary of All Drug-Related Adverse Events by System Organ Class– Maintenance Phase		WK48
3.17.	Safety	AE5B	Summary of All Drug-Related Adverse Events by System Organ Class and Maximum Toxicity – Maintenance Phase	CS Core	HL, WK48
3.18.	Safety	AE5B	Summary of All Drug-Related Adverse Events by System Organ Class and Maximum Toxicity – Maintenance + Extension Phase	CS Core (for Q4W arm only)	WK48, 96, EOS
3.19.	ESP	AE5B	Summary of All Drug-Related Adverse Events by System Organ Class and Maximum Toxicity – Extension Phase	CS Core (for current ART only)	WK48, 96, EOS
3.20.	Safety	AE3	Summary of All Drug-Related Grade 2-5 Adverse Events by Overall Frequency – Maintenance Phase		WK48
Serious and Other Significant Adverse Events					
3.21.	Safety	AE1	Summary of Serious Adverse Events by System Organ Class – Maintenance Phase	CS Core	HL, WK48
3.22.	Safety	AE1	Summary of Serious Adverse Events by System Organ Class – Maintenance +Extension Phase	CS Core(for Q4W arm only)	WK48, 96, EOS

Safety Tables (Displays will be for both treatment arms, unless specified)					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.23.	ESP	AE1	Summary of Serious Adverse Events by System Organ Class – Extension Phase	CS Core(for Current ART arm only)	WK48, 96, EOS
3.24.	LTFU	AE1	Summary of Serious Adverse Events by System Organ Class – Long term follow up	CS Core	WK48, 96, EOS
3.25.	Safety	AE1	Summary of Serious Adverse Events by System Organ Class — Oral Lead-in Period at Maintenance phase	CS Core for Q4W only	HL, WK48
3.26.	Safety	AE1	Summary of Drug-Related Serious Adverse Events by System Organ Class – Maintenance Phase	CS Core	WK48
3.27.	Safety	AE1	Summary of Drug-Related Serious Adverse Events by System Organ Class – Maintenance + Extension Phase	CS Core(for Q4W arm only)	WK48, 96, EOS
3.28.	ESP	AE1	Summary of Drug-Related Serious Adverse Events by System Organ Class – Extension Phase	CS Core(for Current arm only)	WK48, 96, EOS
3.29.	Safety	AE3	Summary of Non-Fatal Serious Adverse Events by Overall Frequency – Maintenance Phase		WK48
3.30.	Safety	AE3	Summary of Drug-Related Non-Fatal Serious Adverse Events by Overall Frequency – Maintenance Phase		WK48
3.31.	Safety	AE1	Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by System Organ Class– Maintenance Phase	CS Core	HL, WK48
3.32.	Safety	AE1	Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by SOC – Maintenance + Extension Phase	CS Core(for Q4W arm only)	WK48, 96, EOS
3.33.	ESP	AE1	Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by SOC – Extension Phase	CS Core(for Current ART arm only)	WK48, 96, EOS

Safety Tables (Displays will be for both treatment arms, unless specified)					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.34.	Safety	AE1	Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by SOC – Oral Lead-in Period at Maintenance Phase	CS Core(for Q4W arm only)	WK48
3.35.	Safety	AE1	Summary of Common (>=5%) Non-Serious Adverse Events – Maintenance Phase	CS Core .	WK48
3.36.	Safety	EudraCT Non-serious AE AE15	Summary of Subjects and Number of Occurrences of Common (>=5%) Non-Serious Adverse Events by System Organ Class – Maintenance Phase	CS Core for FDAAA and EMA disclosure requirements. EudraCT Use macro TD_AE4VCTR for New Data Disclosure HARP Reporting Tools	WK48
3.37.	Safety	EudraCT SAE AE16	Summary of Subjects and Number of occurrences of SAEs, Drug-related AEs, Fatal SAEs, and Drug-related SAEs – Maintenance Phase	CS Core for FDAAA and EMA disclosure requirements. EudraCT	WK48
3.38.	Safety	Shell TS2.1	Summary of Cumulative Adverse Events by Visit– Maintenance Phase	Please note that this table only display AEs occurring >=5% subjects during Maintenance phase	WK48
3.39.	Safety	Shell TS15	Summary of Adverse Events by System Organ Class and Baseline ART Third Agent Class – Maintenance Phase		WK48
Injection Site Reaction Adverse Events					
3.40.	Safety	Shell TS2.2	Summary of Injection Site Reaction Adverse Events (Event-Level Summary) –Maintenance Phase	(for Q4W arm only)	HL, WK48
3.41.	Safety	Shell TS2.2	Summary of Injection Site Reaction Adverse Events (Event-Level Summary) –Maintenance + Extension Phase	(for Q4W arm only)	WK96, EOS
3.42.	ESP	Shell TS2.2	Summary of Injection Site Reaction Adverse Events (Event-Level Summary) –Extension Phase	(for Current ART arm only)	WK96, EOS

Safety Tables (Displays will be for both treatment arms, unless specified)					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.43.	Safety	Shell TS2.3	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events – Overall and Common (Maintenance Phase)	Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects (for Q4W arm only)	WK48
3.44.	Safety	Shell TS2.3	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events – Overall and Common (Maintenance + Extension Phase)	Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects (for Q4W arm only)	WK96, EOS
3.45.	ESP	Shell TS2.3	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events – Overall and Common (Extension Phase)	Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects (for Current ART arm only)	WK96, EOS
3.46.	Safety	Shell TS2.4	Summary of Injection Site Reaction Adverse Events by Visit and Maximum Severity – Overall and Common (Maintenance Phase)	Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects for Q4W arm only)	WK48
3.47.	Safety	Shell TS2.2	Summary of Drug-related Injection Site Reaction Adverse Events (Event-Level Summary) – CAB (Maintenance Phase)	(for Q4W arm only)	WK48
3.48.	Safety	Shell TS2.3	Summary of Drug-related Subject-Level Characteristics of Injection Site Reaction Adverse Events (Maintenance Phase) - Overall and Common (CAB)	Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects (for Q4W arm only)	WK48

Safety Tables (Displays will be for both treatment arms, unless specified)					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.49.	Safety	Shell TS2.4	Summary of Overall and Common Drug-related Injection Site Reaction Adverse Events by Visit and Maximum Severity (Maintenance Phase) - CAB	Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects (for Q4W arm only)	WK48
3.50.	Safety	Shell TS2.5	Summary of Subject-Level Maximum Graded Drug-related Injection Site Reaction Adverse Events by Needle Length (Maintenance Phase) - Common (CAB)	Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects(for Q4W arm only)	WK48
3.51.	Safety	Shell TS2.2	Summary of Drug-related Injection Site Reaction Adverse Events (Event-Level Summary) - RPV (Maintenance Phase)	(for Q4W arm only)	WK48
3.52.	Safety	Shell TS2.3	Summary of Subject-Level Characteristics of Drug-related Injection Site Reaction Adverse Events (Maintenance Phase) - Overall and Common (RPV)	Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects (for Q4W arm only)	WK48
3.53.	Safety	Shell TS2.4	Summary of Overall and Common Drug-related Injection Site Reaction Adverse Events by Visit and Maximum Severity (Maintenance Phase) -RPV	(for Q4W arm only)	WK48
3.54.	Safety	Shell TS2.5	Summary of Subject-Level Maximum Graded Drug-related Injection Site Reaction Adverse Events by Needle Length (Maintenance Phase) - Common (RPV)	Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects (for Q4W arm only)	WK48

Safety Tables (Displays will be for both treatment arms, unless specified)					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Chemistry and Haematology					
3.55.	Safety	LB1	Summary of Chemistry Changes from Baseline by Visit - XXX	CS Core (include lipids and glucose in Conventional Units, renal biomarkers of Retinol Binding Protein, Cystatin C, and CKD-EP1 GFR using Creatinine, and CKD-EP1 using Cystatin C) (for 'WK48' report, XXX is 'Maintenance Phase'; for '96' and 'EOS' report, this table will be split into two: one with 'XXX' being 'Maintenance + Extension Phase for Q4W arm' , and one with 'XXX' being 'Extension Phase for Switching Population'). For lipids, using LOCF data	WK48, 96, EOS
3.56.	Safety	LB1	Summary of Change from Baseline in eGFR using Cystatin C for Subjects Receiving TDF at Baseline	Exploratory (display baseline and Week 48 only)	WK48
3.57.	Safety	LB1	Summary of Change from Baseline in eGFR using Cystatin C by Baseline Third Agent Class	Exploratory (display baseline and Week 48 only)	WK48
3.58.	Safety	Shell TS16	Summary of Fasting Lipids Percentage Changes from Baseline by Visit – Maintenance Phase (LOCF)		WK48
3.59.	Safety	LB1	Summary of Chemistry values by Visit at Maintenance Phase	(include lipids and glucose in Conventional Units, renal biomarkers of Retinol Binding Protein, Cystatin C, et al) For lipids, using LOCF data	WK48,

Safety Tables (Displays will be for both treatment arms, unless specified)					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.60.	Safety	LB1	Summary of Haematology Changes from Baseline by Visit - XXX	CS Core (for 'WK48' report, XXX is 'Maintenance Phase'; for '96' and 'EOS' report, this table will be split into two: one with 'XXX' being 'Maintenance + Extension Phase for Q4W arm' , and one with 'XXX' being 'Extension Phase for Switching Population')	WK48, 96, EOS
3.61.	Safety	Shell TS9.1,	Summary of Maximum Post-Baseline Emergent Chemistry Toxicities - Maintenance Phase	CS Core	WK48
3.62.	Safety	Shell TS9.2	Summary of Maximum Post-Baseline Emergent Chemistry Toxicities – Maintenance + Extension Phase	CS Core (for Q4W arm only)	WK96, EOS
3.63.	ESP	Shell TS9.3	Summary of Maximum Post-Baseline Emergent Chemistry Toxicities - Extension Phase	CS Core (for Current ART arm only)	WK96, EOS
3.64.	Safety (Q4W IM only)	Shell TS9.2	Summary of Maximum Post-Baseline Emergent Chemistry Toxicities – Oral Lead-in Period at Maintenance Phase	CS Core (for Q4W arm only)	WK48
3.65.	Safety	Shell TS9.1,	Summary of Maximum Post-Baseline Emergent Haematology Toxicities - Maintenance Phase	CS Core	WK48
3.66.	Safety	Shell TS9.2	Summary of Maximum Post-Baseline Emergent Haematology Toxicities - Maintenance + Extension Phase	CS Core (for Q4W arm only)	WK96, EOS
3.67.	ESP	Shell TS9.3	Summary of Maximum Post-Baseline Emergent Haematology Toxicities - Extension Phase	CS Core (for Current ART arm only)	WK96, EOS
3.68.	Safety (Q4W IM only)	Shell TS9.2	Summary of Maximum Post-Baseline Emergent Haematology Toxicities - Oral Lead-in Period at Maintenance Phase	CS Core (for Q4W arm only)	WK48

Safety Tables (Displays will be for both treatment arms, unless specified)					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Urinalysis					
3.69.	Safety	UR3 or SHELL TS3	Summary of Urinalysis Dipstick Results by visit - xxx	(for 'WK48' report, XXX is 'Maintenance Phase'; for '96' and 'EOS' report, this table will be split into two: one with 'XXX' being 'Maintenance + Extension Phase for Q4W arm' , and one with 'XXX' being 'Extension Phase for Switching Population')	WK48, 96, EOS
3.70.	Safety	LB1	Summary of Urine Concentrations Changes from Baseline by Visit - xxx	CS Core (including renal biomarkers of Retinol Binding Protein, Albumin/creatinine, Protein/creatinine) (for 'WK48' report, XXX is 'Maintenance Phase'; For '96' and 'EOS' report, this table will be split into two: one with 'XXX' being 'Maintenance + Extension Phase for Q4W arm' , and one with 'XXX' being 'Extension Phase for Switching Population')	WK48, 96, EOS
3.71.	Safety	Shell TS4	Summary of Changes in Proteinuria Baseline Laboratory Result to Maximum Post-Baseline Laboratory Result - Maintenance Phase		WK48
Laboratory: NCEP Lipid and Biomarkers					
3.72.	Safety	Shell TS5	Summary of Changes in NCEP Fasting Lipid Baseline Category to Maximum Post-Baseline Category - Triglycerides - Maintenance Phase		WK48

Safety Tables (Displays will be for both treatment arms, unless specified)					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.73.	Safety	Shell TS5	Summary of Changes in NCEP Fasting Lipid Baseline Category to Maximum Post-Baseline Category – Total Cholesterol - Maintenance Phase		WK48
3.74.	Safety	Shell TS5	Summary of Changes in NCEP Fasting Lipid Baseline Category to Maximum Post-Baseline Category – HDL Cholesterol - Maintenance Phase		WK48
3.75.	Safety	Shell TS5	Summary of Changes in NCEP Fasting Lipid Baseline Category to Maximum Post-Baseline Category – LDL Cholesterol - Maintenance Phase		WK48
3.76.	Safety	Shell TS6	Summary of TC/HDL ratio Changes from Baseline - Maintenance Phase (LOCF Lipid)		WK48
3.77.	Safety	Shell TS7	Summary of Bone Markers Changes from Baseline at week 48		WK48,
3.78.	Safety	Shell TS7	Summary of Bone Markers values at Week 48		WK48,
3.79.	Safety	Shell TS8	Statistical Analysis of bone biomarkers (ratio of week 48 over baseline) - Observed Case		WK48
Laboratory: Hepatobiliary (Liver)					
3.80.	Safety	Liver1 /Shell TS11	Summary of Liver Monitoring/Stopping Event Reporting (Maintenance Phase)		WK48
3.81.	Safety	liver10/Shell TS12	Summary of Subjects Meeting Hepatobiliary Abnormality Criteria - Post-Baseline– Maintenance Phase		WK48
3.82.	Safety	liver10/Shell TS12	Summary of Subjects Meeting Hepatobiliary Abnormality Criteria - Post-Baseline– Maintenance +Extension Phase	(for Q4W arm only)	WK48, 96, EOS
3.83.	ESP	liver10/Shell TS12	Summary of Subjects Meeting Hepatobiliary Abnormality Criteria - Post-Baseline– Extension Phase	(for Current ART arm only)	WK48, 96, EOS
3.84.	Safety (Q4W arm only)	liver10/Shell TS12	Summary of Subjects Meeting Hepatobiliary Abnormality Criteria - Post-Baseline– Oral Lead-in Period at Maintenance Phase	(for Q4W arm only)	WK48

Safety Tables (Displays will be for both treatment arms, unless specified)					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ECG					
3.85.	Safety	EG1	Summary of ECG Findings (Maintenance Phase)		WK48
3.86.	Safety	EG1	Summary of ECG Findings (Maintenance +Extension Phase)	(for Q4W arm only)	WK96, EOS
3.87.	ESP	EG1	Summary of ECG Findings (Extension Phase)	(for Current ART arm only)	WK96, EOS
3.88.	Safety	EG2	Summary of Change from Baseline in ECG values by Visit at Maintenance Phase		WK48
3.89.	Safety	EG2	Summary of Change from Baseline in ECG values by Visit at Maintenance + Extension Phase		WK96, EOS
3.90.	ESP	EG2	Summary of Change from Baseline in ECG values by Visit at Extension Phase		WK96, EOS
3.91.	Safety	EG10	Summary of QTc Values by Category at Maintenance Phase	Mid200056/wk48idsl/Table 8.1043	WK48
3.92.	Safety	EG10	Summary of QTc Values by Category at Maintenance+ Extension Phase	Mid200056/wk48idsl/Table 8.1043 (for Q4W arm only)	WK96, EOS
3.93.	ESP	EG10	Summary of QTc Values by Category at Extension Phase	Mid200056/wk48idsl/Table 8.1043 (for Current ART arm only)	WK96, EOS
3.94.	Safety	EG2	Summary of Change from Baseline QTc Values by Category at Maintenance Phase	Mid200056/wk48idsl/Table 8.1044	WK48
3.95.	Safety	EG2	Summary of Change from Baseline QTc Values by Category at Maintenance+Extension Phase	Mid200056/wk48idsl/Table 8.1044 (for Q4W arm only)	WK96, EOS
3.96.	ESP	EG2	Summary of Change from Baseline QTc Values by Category at Extension Phase	Mid200056/wk48idsl/Table 8.1044(for Current ART arm only)	WK96, EOS
eC-SSR and Others					
3.97.	Safety	VS1	Summary of Change from Baseline in Vital Signs by Visit at Maintenance Phase	CS Core	WK48

Safety Tables (Displays will be for both treatment arms, unless specified)					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.99.	Safety	Shell TS14	Summary of Subjects with Post Baseline eC-SSRS Suicidal Ideation or Behaviour at Maintenance Phase		WK48
3.100.	Safety	Shell TS14.1	Summary of Post Baseline Depression and Suicidal and Self-Injury Adverse Events by System Organ Class, Maximum DAIDS Toxicity Grade, and Prior History of Depression, Anxiety and Suicidal and Self-Injury – Maintenance phase		WK48

13.13.8. Safety Figures

Safety : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
3.1.	Safety	AE10	Plot of Common Adverse Events and Relative Risk-Q4W vs Current ART at Maintenance Phase	CS CORE	HL, WK 48
3.2.	Safety	LIVER9	Scatter Plot of Maximum vs. Baseline for ALT (Maintenance Phase)	CS CORE	HL, WK 48
3.3.	Safety	LIVER9	Scatter Plot of Maximum ALT vs. Maximum Total Bilirubin (Maintenance Phase)	CS CORE	HL, WK 48
3.4.	Safety	Shell FS2/	Matrix Plot of Maximum Liver Chemistries at Maintenance Phase	CS CORE	HL, WK 48
3.5.	Safety	Shell FS3/	Plot of Onset, Duration, and Severity of Overall and Common Maintenance Phase Injection Site Reaction AEs by Maximum Grade: CAB/RPV		WK 48
3.6.	Safety	Shell FS3/	Plot of Onset, Duration, and Severity of Overall and Common Maintenance Phase Injection Site Reaction AEs by Maximum Grade: CAB		WK 48
3.7.	Safety	Shell FS3/	Plot of Onset, Duration, and Severity of Overall and Common Maintenance Phase Injection Site Reaction AEs by Maximum Grade: RPV		WK 48
3.8.	Safety	Shell FS4/	Plot of Incidence of Maintenance Phase Injection Site Reaction Adverse Events-Overall and Common – CAB/RPV		WK 48
3.9.	Safety	Shell FS4/	Plot of Incidence of Maintenance Phase Injection Site Reaction Adverse Events-Overall and Common – CAB		WK 48
3.10.	Safety	Shell FS4/	Plot of Incidence of Maintenance Phase Injection Site Reaction Adverse Events-Overall and Common – RPV		WK 48
3.11.	Safety	Shell FS4/	Plot of Incidence of Grade 3-5 Maintenance Phase Injection Site Reaction Adverse Events - Overall and Common - CAB/RPV		WK 48

Safety : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.12.	Safety	Shell FS4/	Plot of Incidence of Grade 3-5 Maintenance Phase Injection Site Reaction Adverse Events - Overall and Common - CAB		WK 48
3.13.	Safety	Shell FS4/	Plot of Incidence of Grade 3-5 Maintenance Phase Injection Site Reaction Adverse Events - Overall and Common - RPV		WK 48
3.14.	Safety	Shell FS1	Bar Chart of Fasting LIPID NCEP Categories for Triglycerides, Total Cholesterol, and LDL at Week 48 vs. Baseline	Example: arenv/arprod/gsk3365791/mid_dori_ph3/week48/outputs/figure 3.062	WK 48
3.15.	Safety	Shell FS1	Bar Chart of Fasting LIPID NCEP Categories for HDL at Week 48 vs. Baseline		WK 48

13.13.9. Health Outcomes Tables

Health Outcomes : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Perception of iNjection Questionnaire (PIN)					
7.1.	ITT-E	THO2	Proportion of Subjects with each of individual items score in PIN by Visit –LOCF (Maintenance phase)		WK48
7.2.	ITT-E	THO1	Summary of PIN in Domain Scores (Bother of ISRs, Leg movement, Sleep, and Acceptance) and Individual Items Scores (Anxiety before, Pain, Satisfaction, Anxiety After, Willingness) by Visit (Maintenance phase)		WK48
7.3.	ITT-E	THO10	Summary and Statistical Analysis of PIN in Domain Scores (Bother of ISRs, Leg movement, Sleep, and Acceptance) and Individual Items Scores (Anxiety before, Pain, Satisfaction, Anxiety After, Willingness) by Visit - LOCF(Maintenance phase)	Wilcoxon Signed -rank test for analysis of 'Acceptance' only	WK48
7.4.	ITT-E	THO1	Summary of PIN Change from Week 5 in Domain Scores (Bother of ISRs, Leg movement, Sleep, and Acceptance) and Individual Items Scores (Anxiety before, Pain, Satisfaction, Anxiety After, Willingness) by Visit (Maintenance phase)		WK48
7.5.	ITT-E	THO1	Summary of PIN Change from Week 5 in Domain Scores (Bother of ISRs, Leg movement, Sleep, and Acceptance) and Individual Items Scores (Anxiety before, Pain, Satisfaction, Anxiety After, Willingness) by Visit – LOCF (Maintenance phase)		WK48
Health-related quality of Life (HATQoL)					
7.6.	ITT-E	THO2	Proportion of Subjects with (HATQoL) each individual questionnaire item by Visit - LOCF(Maintenance phase)		WK48
7.7.	ITT-E	THO1	Summary of Quality of Life (HATQoL) Score in Life Satisfaction, HIV medication, and Disclosure worries by Visit (Maintenance phase)		WK48

Health Outcomes : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
7.8.	ITT-E	THO1	Summary of Quality of Life (HATQoL) Score in Life Satisfaction, HIV medication, and Disclosure worries by Visit - LOCF(Maintenance phase)		WK48
7.9.	ITT-E	THO1	Summary of Quality of Life Score (HATQoL)-Change from Baseline in Life Satisfaction, HIV medication, and Disclosure worries by Visit (Maintenance phase)		WK48
7.10.	ITT-E	THO1	Summary of Quality of Life Score (HATQoL)-Change from Baseline in Life Satisfaction, HIV medication, and Disclosure Worries by Visit - LOCF(Maintenance phase)		WK48
7.11.	ITT-E	Shell THO3	Statistical Analysis of Quality of Life Score (HATQoL)- Change from Baseline in Life Satisfaction, HIV medication, and Disclosure Worries by Visit – LOCF (Maintenance phase)	ANCOVA for analysis	WK48
Health Status:12-item short form survey (SF-12)					
7.12.	ITT-E	THO2	Proportion of Subjects with SF-12 Individual Item Scores by Visit - LOCF(Maintenance phase)		WK48
7.13.	ITT-E	THO1	Summary of SF-12 (Total Score, MCS and PCS Scores) by Visit) (Maintenance phase)		WK48
7.14.	ITT-E	THO1	Summary of SF-12 (Total Score, MCS and PCS Scores) by Visit - LOCF) (Maintenance phase)		WK48
7.15.	ITT-E	THO1	Summary of Change from Baseline in SF-12 (Total Score, MCS and PCS Scores) by Visit) (Maintenance phase)		WK48
7.16.	ITT-E	THO1	Summary of Change from Baseline in SF-12 (Total Score, MCS and PCS Scores) by Visit - LOCF) (Maintenance phase)		WK48
7.17.	ITT-E	Shell THO3	Statistical Analysis of SF-12 Change from Baseline in Total Score, MCS, and PCS Score by visit – (LOCF)(Maintenance phase)	ANCOVA for analysis	WK48

Health Outcomes : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Treatment Satisfaction (HIVTSQs)					
7.18.	ITT-E	Shell THO2	Proportion of Subjects with HIVTSQs-Treatment Satisfaction Individual Item Scores by Visit - LOCF)(Maintenance phase)		WK48
7.19.	ITT-E	Shell THO2	Proportion of Subjects with HIVTSQs-Treatment Satisfaction Individual Item Scores by Visit and subgroup - LOCF) (Maintenance phase)	The subgroups are Baseline third agent class, Sex at birth, age (<35; 35-<50; ≥50), race, baseline CD4+ as described in Section 5.4	WK48
7.20.	ITT-E	Shell THO1	Summary of HIVTSQs - Total Treatment Satisfaction Score by Visit)(Maintenance phase)		WK48
7.21.	ITT-E	Shell THO1	Summary of HIVTSQs - Total Treatment Satisfaction Score by Visit - LOCF) (Maintenance phase)		WK48
7.22.	ITT-E	Shell THO1	Summary of HIVTSQs - Change from Baseline in Total Treatment Satisfaction Score by Visit)(Maintenance phase)		WK48
7.23.	ITT-E	Shell THO1	Summary of HIVTSQs - Change from Baseline in Total Treatment Satisfaction Score by Visit- LOCF) (Maintenance phase)		WK48
7.24.	ITT-E	Shell THO3	Statistical Analysis of HIVTSQs - Change from Baseline in Total Treatment Satisfaction Score by visit – - LOCF) (Maintenance phase)	ANCOVA for analysis	WK48

Health Outcomes : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Treatment Satisfaction (HIVTSQc)					
7.25.	ITT-E	Shell THO2	Proportion of Subjects with HIV-Treatment Satisfaction Questionnaire Individual Item Scores change) (Maintenance phase)		WK48
7.26.	ITT-E	Shell THO1	Summary of HIV-Treatment Satisfaction Questionnaire in Treatment Satisfaction Score Change)(Maintenance phase)		WK48
7.27.	ITT-E	Shell THO5	Statistical Analysis of HIV-Treatment Satisfaction Questionnaire in Treatment Satisfaction Score Change at Week 48 ())(Maintenance phase)	ANOVA for analysis	WK48

Health Outcomes : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Treatment Acceptance (ACCEPT)					
7.28.	ITT-E	Shell THO2	Proportion of Subjects with Treatment Acceptance Questionnaire(ACCEPT) Individual Item Scores by Visit - LOCF)(Maintenance phase)		WK48
7.29.	ITT-E	Shell THO1	Summary of Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit (Maintenance phase)		WK48
7.30.	ITT-E	Shell THO1	Summary of Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit - LOCF(Maintenance phase)		WK48
7.31.	ITT-E	Shell THO1	Summary of Change from Baseline in Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit (Maintenance phase)		WK48
7.32.	ITT-E	Shell THO1	Summary of Change from Baseline in Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit - LOCF(Maintenance phase)		WK48
7.33.	ITT-E	Shell THO3	Statistical Analysis of Change from Baseline in Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit – LOCF (Maintenance phase)	ANCOVA for analysis	WK48
Tolerability of Injection, NRS (for Q4W IM)					
7.34.	ITT-E	Shell THO2	Proportion of Subjects with Tolerability of Injection (NRS) Individual item scores by Visit - LOCF)(Maintenance phase)		WK48
7.35.	ITT-E	Shell THO9	Summary of Tolerability of Injection(NRS) scores by Visit (Maintenance phase)		WK48
7.36.	ITT-E	Shell THO9	Summary of Tolerability of Injection(NRS) scores by Visit - LOCF) (Maintenance phase)		WK48
7.37.	ITT-E	Shell THO9	Summary of Tolerability of Injection (NRS) by Visit - Change from Week 4B Scores)(Maintenance phase)		WK48

Health Outcomes : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
7.38.	ITT-E	Shell THO9	Summary of Tolerability of Injection (NRS) by Visit - Change from Week 4B Scores - LOCF)(Maintenance phase)		WK48
Preferences (Dichotomous preference question)					
7.39.	ITT-E	Shell THO8	Treatment Preference at Week 48 (Maintenance phase)		W48
Willingness to switch					
7.40.	ITT-E	Shell THO7	Summary of Reasons for Willingness to Switch) (Maintenance phase)		WK48

13.13.10. Health Outcomes Figures

Health Outcomes : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
7.1.	ITT-E	Shell FHO1	Line Plot of Adjusted Mean (95% CI) Change from Baseline in HIVTSQs Total Treatment Satisfaction Score over Time - ANCOVA -LOCF		WK48
7.2.	ITT-E	Shell FHO2	Line Plot of Difference (95% CI) in Adjusted Mean Change from Baseline in HIVTSQs Total Treatment Satisfaction Score over Time - ANCOVA -LOCF		WK48
7.3.	ITT-E	Shell FHO1	Line Plot of Adjusted Mean (95% CI) Change from Baseline in SF-12 (Total, MCS and PCS subscale) Score over Time - ANCOVA - LOCF		WK48
7.4.	ITT-E	Shell FHO2	Line Plot of Difference (95% CI) in Adjusted Mean Change from Baseline in SF-12 (Total, MCS and PCS subscale) Score over Time - ANCOVA -LOCF		WK48
7.5.	ITT-E	Shell FHO1	Line Plot of Adjusted Mean (95% CI) Change from Baseline (HATQoL) in Life Satisfaction, HIV medication, and Disclosure worries by Visit-LOCF ANCOVA		WK48
7.6.	ITT-E	Shell FHO2	Line Plot of Difference in Adjusted Mean (95% CI) Change from Baseline(HATQoL) in Life Satisfaction, HIV medication, and Disclosure worries by Visit-LOCF ANCOVA		WK48

13.13.11. Pharmacokinetic Tables

The 'PK Population' will be used, except where noted. At Week 48 IA, Tables/ Figures will be produced for Q4W IM arm (up to visit of Week 52), At Week 96 IA, Tables/Figures will be produced for Q4W IM arm and for 'Extension Switch Population' (ESP) up to the visit of Week 96, separately, unless otherwise specified.

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes** The similar outputs below from study 200056 (week48idsl), unless otherwise specified	**Deliverable [Priority]**
PK					
4.1.	PK	PKCT1	Summary of Plasma CAB PK Concentration (ug/mL) -Time Data by Treatment and Visit – Included Log-transformed Statistics	Table 10.1010	WK48, 96
4.2.	PK	PKCT1	Summary of Plasma RPV PK Concentration (ng/mL) -Time Data by Treatment and Visit – Included Log-transformed Statistics	Table 10.1011	WK48, 96
4.3.	PK	PKCT1	Summary of Evaluable Plasma CAB PK Concentration (ug/mL)- Time Data by Treatment and Visit – Included Log-transformed Statistics	Table 10.1012	WK48, 96
4.4.	PK	PKCT1	Summary of Evaluable Plasma RPV PK Concentration (ng/mL) - Time Data by Treatment and Visit – Included Log-transformed Statistics	Table 10.1013	WK48, 96
4.5.	PK	Shell TPK01	Summary of Results of Steady State Assessment	Table 10.1005	WK48
4.6.	PK	Shell TPK01	Summary of Results of Steady State Assessment- Evaluable concentration	Table 10.1009,	WK48
4.7.	PK	PKCT1	Summary of Long-Term Follow-up Phase Plasma CAB PK Concentration (ng/mL) -Time Data by Treatment and Visit - Included Log-transformed Statistics	Table 10.1001 (WK96CDISC)	WK96

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes** The similar outputs below from study 200056 (week48idsl), unless otherwise specified	**Deliverable [Priority]**
4.8.	PK	PKCT1	Summary of Long-Term Follow-up Phase Plasma RPV PK Concentration (ng/mL) -Time Data by Treatment and Visit - Included Log-transformed Statistics	Table 10.1002 (WK96CDISC)	WK96

13.13.12. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes** The mock-up below from study 200056 (week48idsl)	**Deliverable [Priority]**
PK					
4.1.	PK	PKCF1	Individual Plasma CAB Concentration-Time Plots (Linear and Semi-Log)	Figure 10.1001	WK48, 96
4.2.	PK	PKCF1	Individual Plasma RPV Concentration-Time Plots (Linear and Semi-Log)	Figure 10.1002	WK48, 96
4.3.	PK	PKCF2	Mean (SD) Plasma CAB Concentration-Time Plots (Linear and Semi-Log)	Figure 10.1003	WK48, 96
4.4.	PK	PKCF3	Median (5th and 95th percentile) Plasma CAB Concentration-Time Plots (Linear and Semi-Log)	Figure 10.1004	WK48, 96
4.5.	PK	PKCF2	Mean (SD) Plasma RPV Concentration-Time Plots (Linear and Semi-Log)	Figure 10.1005	WK48, 96
4.6.	PK	PKCF3	Median(5th and 95th percentile) Plasma RPV Concentration-Time Plots (Linear and Semi-Log)	Figure 10.1006	WK48, 96
4.7.	PK	PKCF2	Mean (SD) Evaluable Plasma CAB Concentration-Time Plots (Linear and Semi-Log)	Figure 10.1007	WK48, 96
4.8.	PK	PKCF3	Median (5th and 95th percentile) Evaluable Plasma CAB Concentration-Time Plots (Linear and Semi-Log)	Figure 10.1008	WK48, 96
4.9.	PK	PKCF2	Mean (SD) Evaluable Plasma RPV Concentration-Time Plots (Linear and Semi-Log)	Figure 10.1009	WK48, 96
4.10.	PK	PKCF3	Median (5th and 95th percentile) Evaluable Plasma RPV Concentration-Time Plots (Linear and Semi-Log)	Figure 10.1010	WK48, 96
4.11.	PK	PKCF2	Mean (SD) Evaluable Plasma CAB Concentration-Time Plots (Semi-Log)	Figure 10.1011	WK48, 96
4.12.	PK	PKCF2	Mean (SD) Evaluable Plasma RPV Concentration-Time Plots (Semi-Log)	Figure 10.1012	WK48, 96

13.13.13. Pharmacokinetic / Pharmacodynamic Tables

The 'PK Population' will be used, except where noted. Tables/ Figures will be produced for Q4W arm only, unless otherwise specified.

Pharmacokinetic / Pharmacodynamic: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell** The similar outputs below from study 200056 (week48idsl)	**Title**	**Programming Notes**	**Deliverable [Priority]**
Last Trough/ Nominal Week 8 Trough CAB/RPV Concentration and efficacy measures					
5.1.					
5.2.	PK	Shell TPK03/Table 11.1007 (subgroup referred to Section 5.4)	Logistic Regression Analysis of Snapshot 'HIV-1 RNA≥50 c/mL' at Week 48 by Trough PK Concentration and subgroup –univariate analysis	Last Trough Concentration and Nominal Week-8 trough PK concentration will be treated both as continuous variable and as subgroup.	WK48
5.3.	PK	Shell TPK03/Table 11.1008	Multivariate Logistic Regression Analysis of Predictors of Snapshot 'HIV-1 RNA≥50 c/mL' at Week 48-		WK48
5.4.	PK	Shell TPK02	Summary of Last trough CAB PK concentration by Virologic Response at Maintenance– Included Log-transformed Statistics	The Virologic Response include: WK48 Snapshot HIV-1 RNA>=50 (Yes/No)	WK48
5.5.	PK	Shell TPK02	Summary of Last trough RPV PK concentration by Virologic Snapshot Response at Week 48 at Maintenance– Included Log-transformed Statistics	Same as above	WK48

Pharmacokinetic / Pharmacodynamic: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell** The similar outputs below from study 200056 (week48idsl)	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.6.	PK	Shell TPK02	Summary of Week-8 trough CAB PK concentration by Snapshot Virologic Response at Week 48 at Maintenance–Included Log-transformed Statistics	The Virologic Response include: WK48 Snapshot HIV-1 RNA>=50 (Yes/No)	WK48
5.7.	PK	Shell TPK02	Summary of Week-8 trough RPV PK concentration by Snapshot Virologic Response at Week 48 at Maintenance–Included Log-transformed Statistics	Same as above	WK48

13.13.14. Pharmacokinetic / Pharmacodynamic Figures

Pharmacokinetic / Pharmacodynamic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell** The similar outputs below from study 200056 (week48idsl)	**Title**	**Programming Notes**	**Deliverable [Priority]**
Last trough/Nominal Week-8 trough CAB/RPV concentration/parameters and efficacy measures					
5.1.	PK	Shell FPK01/Figure 11.1004	Scatter Plot of Last Trough CAB PK Concentration by Snapshot 'HIV-1 RNA≥50' and non-'HIV-1 RNA≥50 c/mL' at Week 48		WK48

Pharmacokinetic / Pharmacodynamic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell** The similar outputs below from study 200056 (week48idsl)	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.2.	PK	Shell FPK01/Figure 11.1005	Scatter Plot of Last Trough RPV PK Concentration by Snapshot 'HIV-1 RNA≥50' and non 'HIV-1 RNA≥50 c/mL' at Week 48		WK48
5.3.	PK	Shell FPK01/Figure 11.1004	Scatter Plot of Week-8 Trough CAB PK Concentration by Snapshot 'HIV-1 RNA≥50' and non-'HIV-1 RNA≥50 c/mL' at Week 48		WK48
5.4.	PK	Shell FPK01/Figure 11.1005	Scatter Plot of Week-8 Trough RPV PK Concentration by Snapshot 'HIV-1 RNA≥50' and non 'HIV-1 RNA≥50 c/mL' at Week 48		WK48
5.5.	PK	Figure 11.1006	Scatter Plot of Delay in last IP injection by Last Trough CAB Concentration at Week 48 at Maintenance phase	Different symbols for Snapshot Non- 'HIV-1 RNA≥50' and 'HIV-1 RNA≥50'. X axis represents last trough CAB concentration, Y axis indicates Delay in last IP injection (Days)	WK48

Pharmacokinetic / Pharmacodynamic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell** The similar outputs below from study 200056 (week48idsl)	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.6.	PK	Figure 11.1006	Scatter Plot of Delay in last IP injection by Last Trough RPV Concentration at Week 48 at Maintenance phase	Different symbols for Snapshot Non- 'HIV-1 RNA≥50' and 'HIV-1 RNA≥50' . X axis represents last trough RPV concentration, Y axis indicates Delay in last IP injection (Days)	WK48
5.7.	PK	Figure 11.1002	Individual CAB trough concentration-time Profiles for subjects with Snapshot HIV-1 RNA≥50 c/mL at Week 48 with Median, 5th & 95th percentile of CAB Conc-Time Profiles for other subjects (Semi-Log)		WK48
5.8.	PK	Figure 11.1003	Individual RPV trough concentration-time Profiles for subjects with Snapshot HIV-1 RNA≥50 c/mL at Week 48 with Median, 5th & 95th CAB Conc-Time Profiles for other subjects (Semi-Log)		WK48
5.9.	PK	Shell FPK02	Scatter plot of Last Trough Concentration of CAB and RPV in relation to occurrence of Snapshot 'HIV-1 RNA≥50 c/mL' at Week 48	Quartiles of CAB and RPV last trough concentration will be marked with vertical and horizontal lines. BMI category will also be marked	W48
5.10.	PK	Shell FPK02	Scatter plot of Week-8 Trough Concentration of CAB and RPV in relation to occurrence of Snapshot 'HIV-1 RNA≥50 c/mL' at Week 48	Same as above	W48

Pharmacokinetic / Pharmacodynamic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell** The similar outputs below from study 200056 (week48idsl)	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration and safety measures					
5.11.	PK	shell FPK03	Scatter Plot of Change from Baseline in 2-Hr QTc versus CAB 2-Hr Post-dose PK Concentrations at Week4B and Week 48	For each visit (i.e. wk4b, 48), produce separate plots of 2-Hr PK concentration vs QTCB and 'overall'. Missing QTCB/QTCF will be derived using RR , if RR is available. For 'overall' plot, if QTCB remains missing with derivation from RR, then other QTC parameters will be used in the order of QTCF, QTC-unspecified, with different colours to differentiate each parameter. (2hr post dose PK concentration at WK4b, week 48 vs CFB in QTC at these two visits)	WK48
5.12.	PK	Shell FPK03	Scatter Plot of Change from Baseline in 2-Hr QTc versus RPV 2-Hr Post-dose PK Concentrations at Week4B and Week 48	Similar to the above for CAB	WK48

Pharmacokinetic / Pharmacodynamic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell** The similar outputs below from study 200056 (week48idsl)	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.13.	PK	shell FPK04	Scatter Plot of Maximum Change from Baseline(CFB) in ALT versus Last Trough CAB PK Concentrations at Maintenance Phase	Last Trough CAB/RPV PK concentration is defined as the most recent trough PK concentration prior or equal to the date of ALT assessment with maximum CFB, at Maintenance phase	Wk48
5.14.	PK	shell FPK04	Scatter Plot of Maximum Change from Baseline(CFB) in ALT versus Last Trough RPV PK Concentrations at Maintenance Phase	Same as above for CAB	Wk48
5.15.	PK	shell FPK04	Scatter Plot of Maximum Change from Baseline(CFB) in Total Bilirubin versus Last Trough CAB PK Concentrations at Maintenance Phase	Last Trough CAB/RPV PK concentration is defined as the most recent trough PK concentration prior or equal to the date of Total Bili assessment with maximum CFB, at Maintenance phase	Wk48
5.16.	PK	shell FPK04	Scatter Plot of Maximum Change from Baseline(CFB) in Total Bilirubin versus Last Trough RPV PK Concentrations at Maintenance Phase	Same as above for CAB	Wk48

Pharmacokinetic / Pharmacodynamic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell** The similar outputs below from study 200056 (week48idsl)	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.17.	PK	shell FPK05	Box Plot of Maximum Toxicity Grades of Most Frequently Reported AEs (e.g. Headache, Fever, Fatigue, Nausea, Dizziness) versus Last Trough CAB PK Concentrations at Maintenance Phase	The AEs for this analysis should be the top 5 in incidence at Maintenance phase. Last Trough CAB/RPV PK concentration is defined as the most recent trough PK concentration prior or equal to the onset date of the most frequently reported AE with maximum toxicity grade, at Maintenance phase. If a subject has no AE most commonly reported, then the last trough value at Maintenance phase will be used for the plot	Wk48
5.18.	PK	shell FPK05	Box Plot of Maximum Toxicity Grades of Most Frequently Reported AEs (e.g. Headache, Fever, Fatigue, Nausea, Dizziness) versus Last Trough RPV PK Concentrations at Maintenance Phase	The same as above	Wk48

13.13.15. Virology Tables

For Week 96/EOS IA, each display will be split into two Tables, one for Maintenance+Extension phases for Q4W arm only, and one for Extension phase for Current ART arm only)					
No.	**Population**	**IDSL / TST ID / Example Shell** (mock up below from study 200056\wk48idsl)	**Title**	**Programming Notes**	**Deliverable**
Genotype					
8.1	CVF	Table 9.1001	Summary of the Prevalence of Known INI Resistance Mutations at time of CVF (Maintenance phase) – Plasma Sample	(identify known INI resistance mutation per Section 13.6.6). need to add small 'n' for actual no. of subjects included in the analysis. The % will be based on 'n' rather than 'N'	WK48
8.2	CVF	Table 9.1003 (modify region to class)	Summary of the Prevalence of Major Resistance Mutations of NRTI, NNRTI and PI Class at time of CVF(Maintenance phase) - - Plasma Sample	(identify Major Mutation of NRTI, NNRTI, PI class per Section 13.6.6). need to add small 'n' for actual no. of subjects included in the analysis. The % will be based on 'n' rather than 'N' (programming for defining class: can refer to arenv/arprod/gsk1349572/mid200304/week24/drivers/t_adpf_4001.sas	WK48
Phenotype					
8.3	CVF	Table 9.1005	Summary of Phenotype Susceptibility at time of CVF (Maintenance phase) - - Plasma Sample		WK48
8.4	CVF	Table 9.1005	Summary of Genotypic Susceptibility at time of CVF (Maintenance phase) - - Plasma Sample		WK48
8.5	CVF	Table 9.1005	Summary of Net Assessment at time of CVF (Maintenance phase) - Plasma Sample		WK48

For Week 96/EOS IA, each display will be split into two Tables, one for Maintenance+Extension phases for Q4W arm only, and one for Extension phase for Current ART arm only)					
No.	**Population**	**IDSL / TST ID / Example Shell** (mock up below from study 200056\wk48idsl)	**Title**	**Programming Notes**	**Deliverable**
8.6	CVF	Table 9.1006	Summary of Phenotype: Number of Drugs to Which Subject are Resistant at time of CVF(Maintenance phase) - Plasma Sample		WK48
8.7	CVF	Table 9.1007	Summary of Phenotypic Susceptibility to CAB and RPV at time of CVF(Maintenance phase) - Plasma Sample		WK48
8.8	CVF	Shell TV1	Summary of Viral load, Genotypic and Phenotypic data for Subjects Who Met Confirmed Virologic Failure Criteria During the Maintenance Phase		HL, WK48
8.9	CVF	Shell TV1	Summary of Viral load, Genotypic and Phenotypic data for Subjects who Met Confirmed Virologic Failure Criteria During the Extension Phase		WK48, 96, EOS
8.10	ITT-E	Shell TV1	Summary of Viral load, Genotypic and Phenotypic data for non-CVF Subjects with genotypic and/or phenotypic data		WK48, 96, EOS

13.13.16. ICH Listings

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population					
1.	Randomised	Shell LSP1	Listing of Subjects Randomised But Not Treated	CS CORE (related to 'Listing for exclusion from any population)	WK48, 96, EOS
2.	Randomised	TA1	Listing of Randomised and Actual Strata and Treatment Assignment	CS CORE	WK48, 96, EOS
3.	All Subjects Screened	ES7	Listing of Reasons for Screen Failure	CS CORE	WK48, 96, EOS
4.	ITT-E	ES2	Listing of Reasons for Study Withdrawal	CS CORE	WK48, 96, EOS
5.	ITT-E	ES2	Listing of Reasons for Study Drug Discontinuation	CS CORE	WK48, 96, EOS
6.	ITT-E	Shell LSP2	Listing of Important Protocol Deviations	CS CORE	WK48, 96, EOS
7.	ITT-E	Shell LSP3	Listing of Protocol Deviations Leading to Exclusion from the Per-Protocol Population	CS CORE	WK48, 96, EOS
8.	ITT-E	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	CS CORE	WK48, 96, EOS
9.	ITT-E	DM2	Listing of Demographic Characteristics	CS CORE	WK48, 96, EOS
10.	ITT-E	DM9	Listing of Race	CS CORE	WK48, 96, EOS
Primary Efficacy					
11.	ITT-E	Shell LPEF1	Listing of Study Outcome (<50 c/mL) at Week 48 – Snapshot Analysis		WK48, 96, EOS

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Secondary Efficacy					
Exposure					
12.	Safety	HIV_IP5	Listing of Investigational Product Exposure Data	CS CORE	WK48, 96, EOS
Adverse Events (the listings below list data for Maintenance + Extension Phases, unless otherwise specified)					
13.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events (Maintenance +Extension phase)	CS CORE	WK48, 96, EOS
14.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event (Maintenance +Extension phase)	CS CORE	WK48, 96, EOS
15.	Safety	AE8	Listing of Fatal Adverse Events (Maintenance +Extension phase)	CS CORE	WK48, 96, EOS
16.	Safety	AE8	Listing of Non-Fatal Serious Adverse Events (Maintenance +Extension phase)	CS CORE	WK48, 96, EOS
17.	Safety	AE8	Listing of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product (Maintenance +Extension phase)	CS CORE	WK48, 96, EOS
18.	Safety	AE8	Listing of changes in intensity/grades of Injection Site Related AE(Maintenance +Extension phase)	Based on AE details inform page, the changes is referring to the same event.	WK48, 96, EOS
19.	Safety	PREG1a	Listing of Subjects Who Became Pregnant During the Study (Maintenance +Extension phase)		WK48, 96, EOS
Hepatobiliary (Liver)					
20.	Safety	MH2	Listing of Medical Conditions for Subjects with Liver stopping Events	IDSL	WK48, 96, EOS
21.	Safety	SU2	Listing of Substance Use for Subjects with Liver Stopping Events	IDSL	WK48, 96, EOS

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ECG & Vital Signs					
22.	Safety	EG3	Listing of ECG Values for subjects with a value of potential clinical concern		WK48, 96, EOS
23.	Safety	EG5	Listing of ECG Findings		WK48, 96, EOS
eC-SSRS					
24.	Safety	PSRAE1	Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Section 1- Section 2		WK48, 96, EOS
25.	Safety	PSRAE3	Listing of Possible Suicidality-Related Adverse Event Data: Possible Cause(s) (Section 3)		WK48, 96, EOS
26.	Safety	PSRAE4	Listing of Possible Suicidality-Related Adverse Event Data (Section 4)		WK48, 96, EOS
27.	Safety	PSRAE5	Listing of Possible Suicidality-Related Adverse Event Data (Section 5- Section 8)		WK48, 96, EOS
PK					
28.	PK pop	Study 200056 Listing 10.1001(wk48idsl)	Listing of Plasma CAB PK Concentration-Time Data	Add a variable of 'evaluable' (Y/N)	WK48, 96, EOS
29.	PK pop	Study 200056 Listing 10.1002(wk48idsl)	Listing of Plasma RPV PK Concentration-Time Data	Add a variable of 'evaluable' (Y/N)	WK48, 96, EOS

13.13.17. Non-ICH Listings

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population					
30.	ITT-E	ES2	Listing of Reasons for Maintenance phase Withdrawal		WK48, 96, EOS
31.	ITT-E	ES2	Listing of Reasons for Oral lead-in Period Withdrawal		WK48, 96, EOS
32.	ESP	ES2	Listing of Reasons for Extension phase Withdrawal		WK48, 96, EOS
33.	LTFU	ES2	Listing of Reasons for Long-term follow up Withdrawal		WK48, 96, EOS
34.	ITT-E	CM3	Listing of ART Medications Stopped Prior to Screening		WK48, 96, EOS
35.	ITT-E	CM3	Listing of ART Medications Received during Screening		WK48, 96, EOS
36.	ITT-E	CM3	Listing of ART Medications Received during LTFU phase		WK48, 96, EOS
37.	ITT-E	CM3	Listing of subjects with changes in Concomitant ARTs during Maintenance phase		WK48, 96, EOS
38.	ITT-E	CM3	Antiretroviral Therapy Taken Prior to & during Screening for Subjects Failing ART Eligibility Criteria	ART Eligibility Criteria are inc2, Exc 3, 4, 5, 6, 34, 36, 37. Please add footnote to this listing describing the details of these criteria (i.e. values of IETESTCD, IETEST)	WK48, 96, EOS
39.	ITT-E	Shell LSP11	Listing of Investigational Product Accountability		WK48, 96, EOS
Secondary Efficacy					
40.	CVF	Shell LSEF3	Listing of All Plasma HIV-1 RNA data for subjects with Confirmed Virologic Failure		WK48, 96, EOS
41.	ITT-E	Shell LSEF1	Listing of All Plasma HIV-1 RNA data for subjects with post-baseline viral load >=50 c/mL		WK48, 96, EOS

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
42.	ITT-E	Shell LSEF1	Listing of Plasma All HIV-1 RNA data for subjects with post-baseline viral load >=50 c/mL at Oral lead-in period		WK48
43.	ITT-E	Shell LSEF5	Listing of HIV-1 Associated Conditions at Maintenance + Extension Phase		WK48, 96, EOS
Safety (The Safety listings below list data for Maintenance + Extension Phases, unless otherwise specified)					
44.	Safety	ABC_HSR _EXPO2	Listing of Abacavir Hypersensitivity Reaction Record - Exposure to Abacavir		WK48, 96, EOS
45.	Safety	ABC_HSR _DRUG2	Listing of Abacavir Hypersensitivity Reaction Record - Subject History of Drug Allergies		WK48, 96, EOS
46.	Safety	ABC_HSR COND2	Listing of Abacavir Hypersensitivity Reaction Record - Subject and Family Conditions		WK48, 96, EOS
47.	Safety	ABC_HSR _RASH2	Listing of Abacavir Hypersensitivity Reaction Record - Skin Rash Details		WK48, 96, EOS
48.	Safety	ABC_HSR _SYMP4	Listing of Abacavir Hypersensitivity Reaction Record - Symptoms		WK48, 96, EOS
49.	Safety	VS4	Listing of Abacavir Hypersensitivity Reaction Record - Vital Signs		WK48, 96, EOS
50.	Safety	ABC_HSR _SYMP6	Listing of Abacavir Hypersensitivity Reaction Record - Individual Symptoms and Diagnostic Category Assignments (Excluding Other Symptoms)		WK48, 96, EOS
51.	Safety	ABC_HSR _SYMP7	Listing of Abacavir Hypersensitivity Reaction Record - Individual Symptoms and Diagnostic Category Assignments (Other Symptoms)		WK48, 96, EOS
52.	Safety	LIVER5	Listing of Liver monitoring/stopping Event reporting		WK48, 96, EOS
53.	Safety	LIVER6	Listing of Liver Event Information for RUCAM Score		WK48, 96, EOS
54.	Safety	LIVER7	Listing of Liver Biopsy Details		WK48, 96, EOS
55.	Safety	LIVER8	Listing of Liver Imaging Details		WK48, 96, EOS

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
56.	Safety	Liver13	Listing Subjects Meeting Hepatobiliary Lab Criteria post-baseline at Maintenance Phase	Please also add those additional items shown in the summary of subjects meeting hepatobiliary lab criteria post-baseline (i.e. AST >3xULN and ALP <2xULN and BIL >=2xULN]; ALT+AST>=xx)	WK48
57.	Safety	AE8	Listing of Adverse Events Potentially Related to Torsades de Pointe		WK48, 96, EOS
58.	Safety	EG3	Listing of ECG values for subjects with Adverse Events Potentially Related to Torsades de Pointes		WK48, 96, EOS
59.	Safety	Liver13	Listing Subjects Meeting Hepatobiliary Lab Criteria post-baseline at Maintenance + Extension Phase for Q4W arm		WK48, 96, EOS
60.	ESP	Liver13	Listing Subjects Meeting Hepatobiliary Lab Criteria post-baseline at Extension Phase (for Current ART arm)		WK48, 96, EOS
61.	Safety	Liver13	Listing Subjects Meeting Hepatobiliary Lab Criteria post-baseline at Oral lead-in Maintenance Phase (for Q4W arm)		WK48
62.	Safety	Latte2 WK96CDISC report	Listing of Each Subjects ALT, AST, Bilirubin (including total and direct Bilirubin), INR, and ALP for subject meeting Hepatobiliary Lab abnormality criteria	8.1037 (add AST, ALP, INR, and direct Bilirubin to the listing and only for subject meeting Hepatobiliary Lab abnormality criteria)	WK48, 96, EOS
63.	Safety	Latte2 WK96CDISC report	Listing of Investigational Product Exposure Data for Subject Receiving Oral Bridging	8.1038	WK48, 96, EOS
Virology (mock up below from study 200056\wk96cdisc), 'Study phase' will be added as a column to the listing.					
64.	ITT-E	Listing 9.1005	Listing of Replication Capacity in IN and PR/RT Region		WK48, 96, EOS

13.14. Appendix 14: IDMC

An IDMC was instituted to perform a triggered periodic review of the accumulating data based on confirmed virologic failures to ensure that subjects are not being sub-optimally treated. In addition, the IDMC will review a futility analysis when 50% of subjects will have reached their Week 24 visit.

A list of outputs required for each IDMC analysis was provided in the IDMC Charter, Section 12.3, Appendix C.

Data handing methods and derived data definitions will be the same as detailed in this RAP, unless otherwise stated.

13.14.1. Adhoc CVF

The number of subjects meeting Confirmed Virologic Failure (CVF) Criterion per the protocol will be monitored and may result in ad-hoc IDMC data reviews.

The Statistics Data Analysis Centre (SDAC) will be notified by the study virologist in writing every time a CVF occurs in either study. The SDAC will track the number of subjects past Week 4. The rate of CVF will be monitored against the thresholds specified in IDMC Charter Table 1 (See IDMC Charter, Section 3.5.2).

13.14.2. Futility Interim

An interim futility analysis for the purpose of review by the IDMC will be performed for this study when about 50% of subjects will have reached their Week 24 visit.

For this Futility Interim, the primary efficacy measure to be reviewed was the proportion of subjects presenting with HIV-1 RNA ≥50 copies/mL at 24 weeks using a Snapshot analysis. A futility rule based on the Bayesian posterior predictive probability approach was applied to assess the evidence that the Q4W IM treatment arm is non-inferior to the current antiretroviral regimen (Current ART) arm given the interim data, at a 6% non-inferiority margin.

13.14.2.1. Futility analysis

An interim analysis for the purpose of review by the IDMC will be performed.

A futility rule will assess the evidence that the CAB LA + RPV LA treatment arm is non-inferior to the control arm (CAR). This rule will use the interim data (50% completing Week 24) to calculate the Bayesian predictive probabilities that the CAB LA + RPV LA arm is non-inferior to the CAR arm. A 6% non-inferiority margin will be used for this study.

For this analysis of CAB LA + RPV LA snapshot 'HIV-1 RNA≥50'rate relative to CAR, let:

X^{I}_{CR} = number of snapshot 'HIV-1 RNA≥50'at interim in CAB LA + RPV LA arm,

N^{I}_{CR} = number of subjects on CAB LA + RPV LA arm at interim,

X^{I}_{CAR} = number of 'HIV-1 RNA≥50'at interim in Triumeq/current ART arm, and

N^{I}_{CAR} = number of subjects on Triumeq/current ART at interim.

Since the true response rate is unknown, prior distributions are placed on these parameters of interest to reflect current beliefs and balanced with acceptable decision criteria performance. Conjugate beta densities are assumed. Since we are anticipating rather large sample sizes at the interim, we simply chose Jeffrey's priors for the response rates (Beta(0.5,0.5)), leading to the posterior distributions on the response rates, based on the interim data:

$P_{CR} \sim \text{Beta}\ (0.5 + X^{I}_{CR},\ N^{I}_{CR} + 0.5 - X^{I}_{CR})$,

$P_{CAR} \sim \text{Beta}\ (0.5 + X^{I}_{CAR},\ N^{I}_{CAR} + 0.5 - X^{I}_{CAR})$.

The posterior predictive probability distribution of the final response data given the final sample sizes:

X^{F}_{CR} = number of snapshot 'HIV-1 RNA≥50' in the final dataset in CAB LA + RPV LA arm,

N^{F}_{CR} = number of subjects on CAB LA + RPV LA arm at the final analysis,

X^{F}_{CAR} = number of 'HIV-1 RNA≥50' in the final dataset in Triumeq/current ART arm

N^{F}_{CAR} = number of subjects on Triumeq/current ART arm at the final analysis.

The number of future observed 'HIV-1 RNA≥50' in each arm follows a beta-binomial distribution:

$$X^{F}_{CR} - X^{I}_{CR} | X^{I}_{CR} \sim \text{beta-binomial}\ (N^{F}_{CR} - N^{I}_{CR},\ 0.5 + X^{I}_{CR},\ 0.5 + N^{I}_{CR} - X^{I}_{CR})$$

$$X^{F}_{CAR} - X^{I}_{CAR} | X^{I}_{CAR} \sim \text{beta-binomial}\ (N^{F}_{CAR} - N^{I}_{CAR},\ 0.5 + X^{I}_{CAR},\ 0.5 + N^{I}_{CAR} - X^{I}_{CAR})$$

The posterior predictive probability (PPP) with a 6% for study individual study, is:

$$PPP = \sum_{X^{F}_{CR}, X^{F}_{CAR}} P(X^{F}_{CR} - X^{I}_{CR} | X^{I}_{CR}) P(X^{F}_{CAR} - X^{I}_{CAR} | X^{I}_{CAR}) I\left(\frac{\hat{p}_{CR} - \hat{p}_{CAR} - (0.06)}{\sqrt{\frac{\hat{p}_{CR}(1-\hat{p}_{CR})}{N^{F}_{CR}} + \frac{\hat{p}_{CAR}(1-\hat{p}_{CAR})}{N^{F}_{CAR}}}} < -1.96\right)$$

where $\hat{p}_{CR} = \frac{X^{F}_{CR}}{N^{F}_{CR}}$, $\hat{p}_{CAR} = \frac{X^{F}_{CAR}}{N^{F}_{CAR}}$ and I is an indicator taking the value 0 or 1. If PPP is less than the targeted threshold (15%), this would signal an IDMC review for futility. Table 22 shows the point at which a futility review would be triggered for a range of virologic failure rates on each arm for this study.

Table 22 Posterior predictive probability (PPP) of determining non-inferiority for individual study (50% subjects reaching wk24). Shaded cells denote the scenarios that would be below the 15% futility criteria (6% non-inferiority Margin).

PPP		No. (%) of 'HIV-1 RNA≥50' (per FDA Snapshot algorithm) on CAB LA+RPV LA , out of 143							
		7 (5%)	**8 (6%)**	**9 (6%)**	**10 (7%)**	**11 (8%)**	**12 (8%)**	**13 (9%)**	**14 (10%)**
No. (%) of 'HIV-1 RNA≥50' (per FDA's Snapshot) on Comparator arm, out of 143	**0**	17.3	6.1	1.5	0.3	0	0	0	0
	1 (1%)	30.6	14.5	5.5	1.7	0.4	0.1	0	0
	2 (1%)	43.8	25.3	12.2	5.0	1.7	0.5	0.2	0
	3 (2%)	57.3	38.0	21.8	10.7	4.6	1.8	0.6	0.2
	4 (3%)	68.5	50.5	32.9	18.9	9.6	4.3	1.8	0.7
	5 (3%)	77.8	62.3	45.0	29.1	16.8	8.8	4.2	1.8
	6 (4%)	85.0	72.5	56.8	40.5	26.2	15.4	8.3	4.1
	7 (5%)	90.3	80.8	67.6	52.2	37.0	24.0	14.3	7.8
	8 (6%)	93.9	87.1	76.7	63.2	48.3	34	22.1	13.3

13.15. Appendix 15: Variables Defined for Time to Event Analysis

TRDF Detailed steps		
The steps below are for the derivation of TRDF i.e. for the Kaplan-Meier analysis only.		
Condition	Censor Status	Event Description/AVAL
1. Subjects met CVF event criteria during the Maintenance Phase. (Based on derived CVF)	CNSR=0	EVNTDESC=CVF AVAL=Date of SVF* *: immediately preceding CVF.
2. Subjects with study withdrawal due to 'Lack of efficacy', 'Treatment related AE', 'intolerability due to injection', or 'protocol defined Safety stopping criteria' during Maintenance phase Note: primary reason for discontinuation based on Maintenance Conclusion Page. 'Treatment related AE' is defined as subjects that have primary reason for withdrawal =AE and that the subject has at least one AE considered drug related (AEREL=Y) and was withdrawn from study (AEWD=Y))	CNSR=0	EVNTDESC= terms in italic, respectively. For ART arm: AVAL= min (Date of Maintenance phase discontinuation, Date of Maintenance Current ART Stop Date + 1) For Q4W arm: AVAL= min [Date of Maintenance phase discontinuation, max(Date of Last Q4W IM Dose + 35, Last Oral dose Date + 1)] Note: Last Q4W IM / last oral dose/ Maintenance Current ART Stop Date is only applied to subjects who permanently discontinue from study treatment Note: Date of Maintenance phase discontinuation is from Maintenance phase Conclusion page
If none of the above conditions met		
3. subjects withdraw during Maintenance Phase	CNSR=1	EVNTDESC='Censored due to Study Discontinuation for Other Reasons' AVAL will be defined as the same as above 2
4 . others	CNSR=1	EVNTDESC='Censored due to data cutoff for analysis' AVAL = End date of on-treatment maintenance phase Which will be defined as below: For Q4W min [week 52 visit date, HAART start date, last contact date, max(date of last Q4W IM dose+35, last oral dose date+1)] For Current ART min [week 52 visit date, last contact date, Current ART stop date+1]

The same approach as will be used to define 'ERDF' except that the reason of withdrawal in Condition 2 will be restricted to 'Lack of Efficacy'.

13.16. Appendix 16: Example Mock Shells for Data Displays

Data Display Specification will be made available on Request.