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

| | | |
|---|---|---|
| **Title** | : | 201584: A Phase III, Randomized, Multicenter, Parallel-group, Open-Label Study Evaluating the Efficacy, Safety, and Tolerability of Long-Acting Intramuscular Cabotegravir and Rilpivirine for Maintenance of Virologic Suppression Following Switch from an Integrase Inhibitor Single Tablet Regimen in HIV-1 Infected Antiretroviral Therapy Naive Adult Participants |
| **Compound Number** | : | GSK1265744 |
| **Effective Date** | : | 17-SEP-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 201584
- This version of the RAP includes amendments to the originally approved RAP
- 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 201584.

| GlaxoSmithKline Document Number | Date | Version |
|---|---|---|
| 2015N248866_00 | 2016-MAY-26 | Original |
| 2015N248866_01 | 2016-DEC-13 | Amendment No. 1 |
| The reasons for this amendment were to: added new primary Medical Monitor contact information; added lipid objective and endpoint back in to the table within the Synopsis section; added clarification of text for patient reported outcome endpoints; added additional clarification regarding provision of CAB LA and RPV LA until available through public/government health sectors; new text added to allow use of local labs to determine eligibility in exceptional circumstances; updated Time and Events Table to provide more clarity around assessments conducted during the Extension Phase, added 'X' to include collection of cardiovascular risk information at Screening, added temperature to Vital Signs row, added row for randomization, and clarified timings for completion of patient reported questionnaires relative to other clinical assessments in the table footnotes; clarified timing of dosing for abacavir/dolutegravir/lamivudine (ABC/DTG/3TC, Triumeq) for the Day 1 visit; added additional clarification that participants of child bearing potential must continue contraception for at least 52 weeks after the last injection; revised text to say that Investigators may provide 'bridging' supply after consultation with Medical Monitor (vs Medical Monitor authorizing bridging supply); provided clarification that cabotegravir and rilpivirine exposure may persist for more than one year in some participants after intramuscular administration (with added references); minor edits to prohibited medication information; added statement that drugs that cause Torsade de Pointes should be used with caution when taking rilpivirine; additional clarification that background NRTI therapy is not considered Investigational Product and accountability will not be done for NRTI background; changed film coat color for Tivicay (dolutegravir) from white (clinical trial material supply) to yellow (commercial supply) and removed statement to "protect from light" (for both Triumeq and Tivicay); sentence added for collection of additional details for the injection device used for IM administration; additional information included regarding randomization schedule; added text stating the investigator must discuss long-term commitment for the study with potential participants; added statement regarding serofast RPR results; allowed serum pregnancy testing where required locally (e.g. when urine testing is not available); removed duplicate text regarding monitoring for suicidal related events; added option for patient reported outcomes to be collected on paper instrument if needed; removed information in Appendix requiring collection of pregnancy information for female partners of male study participants; definition of ACCEPT, HIVTSQc, and HIVTSQs added to abbreviations table, duplication of ICH abbreviation removed; other minor corrections (e.g., updated references, adding cross reference to sections, correction of hyperlink to one table). | | |

| | | |
|---|---|---|
| 2015N248866_02 | 2017-JUL-19 | Amendment No. 2 |
| The reasons for this amendment are as follow: update of contact information for secondary Medical Monitor; modify text to allow dose reduction for participants who have a decline in creatinine clearance to <50 mL/min; clarify that for participants not eligible to continue into the Maintenance Phase, only samples with HIV-1 RNA > 400 c/mL will be sent for resistance testing; add mitigation for ECG pad removal; clarify ± 3 day window is for all oral dosing (both Induction and Maintenance Phase); add "LA Arm" back to columns for Week 68, 76, 84, 92 on Time and Events Schedule (hidden when column was narrowed); clarify Week 104b visit is specific to those participants transitioning from oral IP to CAB LA + RPV LA; clarification added to footnote 'p' that genetics sample can be collected at any visit after signing informed consent, but Week [-20] preferred; correct footnote on Week 5 visit to reflect footnote 't'; add footnote 'y' back to Time and Events column for Withdrawal Visit (for Induction Phase); add clarification to Time and Events column that ISR assessments are only conducted for participants receiving injections; remove text from Section 12.2: 'In addition, all deaths related to an AE are to be classified as grade 5.' Administrative typographical errors corrected (e.g. clarification provided regarding genetics sample taken after participants are enrolled into the study [vs when participants are randomized]), and investigator brochure references updated. | | |
| 2015N248866_03 | 2018-JUN-25 | Amendment No. 3 |
| Changes for Amendment 3 were made to the protocol to manage and mitigate risks following identification of a potential safety issue related to neural tube defect in infants born to women with exposure to dolutegravir (DTG) at the time of conception.<br><br>A Risk Assessment table was added to include language regarding risk and mitigation of neural tube defects seen with DTG.<br><br>• The withdrawal criteria were updated to include a reminder that females of reproductive potential who change their minds and desire to be pregnant should also be withdrawn from the study.<br>• The Time and Events table was updated to include a reminder for investigators to check at every visit that females of reproductive potential are avoiding pregnancy.<br>Additionally, clarifications were provided for the following:<br>• the DTG IB should be referenced for additional risks, safety information, drug interactions, etc.;<br>• 'suspected' was added to the text prior to the bulleted definition of suspected virologic failure in Section 5.4.5.3.;<br>• specific storage conditions were removed from the protocol for IP, and a statement added to store according to product label;<br>• insulin was removed from the section regarding clinical assessments performed during the study;<br>• timeframe for pregnancy reporting and follow-up were updated to 24 hours to align with current reporting process;<br>• prescribing information and IB references were updated. | | |

## 1.1. RAP Amendments

Revision chronology:

| RAP Section | Amendment Details |
|---|---|
| **Reporting and Analysis Plan_201584_Final_V1 [17-AUG-2018]** | |
| **Reporting and Analysis Plan_201584_Amendment_Final_V1 [17-SEPT-2018]** | |

# 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 #3 [(Dated: 25/JUN/2018)].

**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** | |
| To demonstrate the non-inferior antiviral activity of switching to intramuscular CAB LA + RPV LA every 4 weeks (monthly) compared to continuation of ABC/DTG/3TC over 48 weeks in HIV-1 antiretroviral naïve participants. | • Proportion of participants with a 'virologic failure' endpoint as per FDA Snapshot algorithm at Week 48 (Missing, Switch, or Discontinuation = Failure, Intent-to-Treat Exposed [ITT-E] population). |
| **Secondary** | |
| To demonstrate the antiviral and immunologic activity of switching to intramuscular CAB LA + RPV LA every 4 weeks (monthly) compared to continuation of ABC/DTG/3TC. | • Proportion of participants with Plasma HIV-1 RNA <50 copies/mL (c/mL) at Week 48 using the FDA Snapshot algorithm (Intent-to-Treat Exposed [ITT-E] population).<br>• Proportion of participants with plasma HIV-1 RNA <200 c/mL at Week 48 using the FDA Snapshot algorithm (ITT-E population).<br>• Proportion of participants with plasma HIV-1 RNA <200 c/mL and HIV-1 RNA <50 c/mL at Week 96 using the FDA Snapshot algorithm (ITT-E population).<br>• Proportion of participants with a 'virologic failure' endpoint as per FDA Snapshot algorithm at Week 96.<br>• Proportion of participants with confirmed |

| Objectives | Endpoints |
|---|---|
| | virologic failure at Week 48 and Week 96.<br>• Absolute values and change from Baseline in plasma HIV-1 RNA ($log_{10}$ copies/mL) at Week 48 and Week 96.<br>• Absolute values and changes from Baseline in CD4+ cell counts over time including Week 48 and Week 96.<br>• Incidence of disease progression (HIV-associated conditions, acquired immunodeficiency syndrome [AIDS] and death). |
| To evaluate the safety and tolerability of switching to CAB LA + RPV LA every 4 weeks (monthly) compared to continuation of ABC/DTG/3TC over time. | • Incidence and severity of adverse events (AEs) and laboratory abnormalities over time including Week 48 and Week 96.<br>• Proportion of participants who discontinue treatment due to AEs over time including Week 48 and Week 96.<br>• Absolute values and changes in laboratory parameters over time including Week 48 and Week 96. |
| To evaluate the effects of CAB LA + RPV LA every 4 weeks on fasting lipids over time compared to continuation of ABC/DTG/3TC over time. | • Change from Baseline in fasting lipids over time including Week 48 and Week 96. |
| To assess the development of viral resistance in participants experiencing protocol-defined virologic failure. | • Incidence of treatment emergent genotypic and phenotypic resistance to CAB, RPV, and other on-study ART at Week 48 and Week 96. |
| To characterize CAB and RPV concentrations and population pharmacokinetics (PK) 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]).<br>• Demographic parameters including, but not limited to, age, sex, race, body weight, body mass index (BMI), and relevant laboratory parameters will be evaluated as potential predictors of inter- and intra-participant variability for pharmacokinetic parameters. |

| Objectives | Endpoints |
|---|---|
| To assess the acceptance of pain and injection site reactions following injections. | • Change from Week 5 in Dimension scores (e.g., "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).<br>• 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 treatment satisfaction of CAB LA + RPV LA compared to continuation of ABC/DTG/3TC. | • Change from baseline in total "treatment satisfaction" score, and individual item scores of the HIV Treatment Satisfaction Questionnaire (status version) (HIVTSQs) at Week 4b, Week 24, Week 44, Week 96 (or Withdrawal).<br>• Change in treatment satisfaction over time (using the HIVTSQc change version [HIVTSQc]) at Week 48 (or Withdrawal). |
| To assess degree of health-related quality of life (HR QoL). | • Change from Baseline in HR QoL using the HIV/AIDS targeted quality of life questionnaire (HAT-QoL) short format Week 24, Week 48, Week 96 (or Withdrawal). |
| To assess 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 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. |

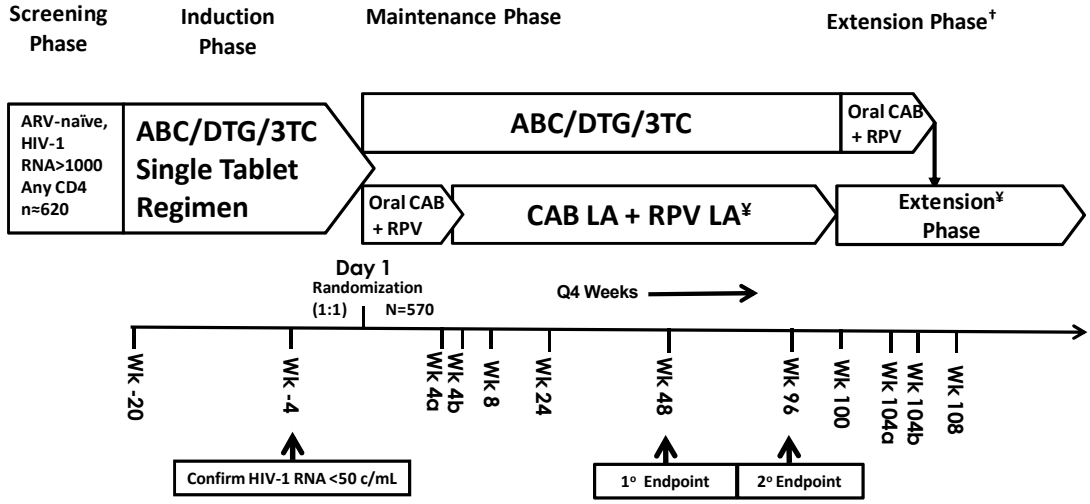
| Objectives | Endpoints |
|---|---|
| To assess tolerability of injections. | • Change from Week 4b in tolerability of injections at Week 5, Week 40, Week 41, and Week 96 using the Numeric Rating Scale (NRS) within the CAB LA + RPV LA arm. |
| **Exploratory** | |
| To evaluate the antiviral and immunologic effects, safety and tolerability, and viral resistance of CAB LA + RPV LA for all participants in the Extension Phase. | • Proportion of participants with plasma HIV-1 RNA <200 c/mL and HIV-1 RNA <50 c/mL over time.<br>• Proportion of participants with confirmed virologic failure over time.<br>• Incidence of treatment emergent genotypic and phenotypic resistance to CAB and RPV in over time.<br>• Absolute values and change from Baseline in plasma HIV-1 RNA over time.<br>• Absolute values and changes from Baseline in CD4+ cell counts over time.<br>• Incidence of disease progression (HIV-associated conditions, acquired immunodeficiency syndrome [AIDS] and death).<br>• Incidence and severity of AEs and laboratory abnormalities over time.<br>• Proportion of participants who discontinue treatment due to AEs over time.<br>• Absolute values and changes in laboratory parameters over time. |
| To explore the effect of participant characteristics on the virologic and immunologic response of CAB LA and RPV LA compared to continuation of ABC/DTG/3TC. | • 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, and 96 using the Snapshot algorithm for the ITT-E population.<br>• Proportion of participants by subgroup(s) (e.g. by age, gender, BMI, race, HIV-1 subtype, Baseline CD4+) with plasma HIV-1 RNA <50 c/mL at Week 48 and Week 96.<br>• Change from Baseline in CD4+ cell counts |

| Objectives | Endpoints |
|---|---|
| | by subgroups at Week 48 and Week 96. |
| 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 receiving CAB LA and RPV LA compared to continuation of ABC/DTG/3TC over time. | • Absolute values and change from Baseline in renal (in urine and blood) and bone (in blood) biomarkers over time including Week 48 and Week 96. |
| To assess preference for CAB LA + RPV LA compared to oral antiretroviral (ARV) therapy using a single dichotomous preference question. | • For participants randomized to the "CAB LA + RPV LA" arm, preference for CAB LA + RPV LA compared to oral ARV regimen, at Week 48. |

## 2.3. Study Design

**Overview of Study Design and Key Features**

**FLAIR (201584)**




†Optional switch to CAB LA + RPV LA at Wk 100 for subjects randomized to ABC/DTG/3TC.
¥Subjects who withdraw from IM CAB LA + RPV LA treatment must enter the 52 week long term follow up phase.

| | |
|---|---|
| **Design Features** | • A Phase III, Randomized, Multicenter, Parallel-group, Open-Label, Switch from an Integrase Inhibitor Single Tablet Regimen in HIV-1 Infected Antiretroviral Therapy Naive Adult Participants<br>• The FLAIR study comprises a Screening Phase (up to 35 days), an Induction Phase (Week [-20] to Day 1), a Maintenance Phase (Day 1 to Week 100), followed by an Extension Phase (post Week 100). 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** | • Induction Phase: oral ABC/DTG/3TC<br>• Maintenance Phase: 1:1 randomization to CAB LA + RPV LA vs. continue oral ABC/DTG/3TC.<br>• Extension Phase: CAB LA + RPV LA |
| **Time & Events** | • Refer to Appendix 2: Schedule of Activities |
| **Treatment Assignment** | • N =570 randomized at start of Maintenance Phase<br>• At Week 100, participants randomised to the oral ABC/DTG/3TC arm meeting eligibility requirements will switch to CAB LA + RPV LA<br>• GSK RandAll NG used to generate randomization schedules<br>• Stratified Randomization by participants' Induction Baseline HIV-1 RNA (<100,000, ≥ 100,000 c/mL) and gender at birth. |

| Overview of Study Design and Key Features | |
|---|---|
| **Interim Analysis** | • IDMC analyses:<br>  • Futility analysis at 50% of participants completing Week 24 Continuous time monitoring of confirmed virologic withdrawal (CVF) until all participants complete Week 24<br>• No study summary data according to actual randomized treatment groups will be available to sponsor staff prior to the planned Week 48 analysis. |
| **Planned Sponsor Analyses** | • The main analysis will be conducted to evaluate the primary objective of the study at Week 48.<br>• An additional planned analysis at Week 96 will be conducted to evaluate long-term antiviral activity, safety, and tolerability and participant satisfaction of the regimens.<br>• Further data cuts and analyses may be conducted as necessary in order to support regulatory submissions and publications. |

## 2.4. Statistical Hypotheses / Statistical Analyses

This study is designed to show that the antiviral effect of oral ABC/DTG/3TC followed by intramuscular CAB LA + RPV LA regimen is non-inferior to continuation of ABC/DTG/3TC at Week 48 of maintenance treatment. Non-inferiority in the proportion of participants with HIV-1 RNA ≥ 50 c/mL at Week 48 for Intent-to-Treat Exposed (ITT-E) population (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 participants with HIV-1 RNA ≥ 50 c/mL between the two treatment arms (CAB – ABC/DTG/3TC) is less than 6%.

If $f_{la}$ is the proportion of participants with HIV-1 RNA ≥ 50 c/mL for the Q4W IM arm and $f_c$ is the proportion of participants with HIV-1 RNA ≥ 50 c/mL (per FDA snapshot algorithm) for the ABC/DTG/3TC arm then the hypotheses can be written as follows:

$$H_o: f_{la} - f_c \geq 6\% \quad H_1: f_{la} - f_c < 6\%$$

# 3. PLANNED ANALYSES

At least two analyses will be conducted to evaluate primary and secondary objectives of the protocol, one after all participants 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. No adjustment for multiplicity caused by repeated evaluation of the primary endpoint will be made as the Week 96 analyses will be secondary.

## 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 participants and to protect the scientific validity of this study and study 201585.

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 demonstrate non-inferiority to the continued ABC/DTG/3TC 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 participants complete Week 24 to ensure that participants are not being sub-optimally treated in the CAB + RPV 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 participants 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.

A secondary analysis will be conducted at Week 96 and a final End-of-Study analysis will be conducted when all participants have completed the study.

# 4. ANALYSIS POPULATIONS

| Population | Definition / Criteria | Analyses Evaluated |
|---|---|---|
| All Subjects Screened Population | • Comprised of all participants screened for inclusion in the study.<br>• Participants may be re-screened once, for which they will receive a new subject number.<br>• Only the latest re-screening data will be included in the screening population summaries/analyses. | • Study Population |
| All Participants Enrolled | • All enrolled participants who receive at least one dose of study drug in the Induction Phase. | • 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).<br>• Participants will be analyzed according to the randomized treatment regardless of what treatment was actually received. | • Study Population<br>• Efficacy |
| Per-Protocol Exposed (PP) | • Consist of all participants in the ITT-E Population with the exception of major protocol violators.<br>• Protocol deviations that would exclude participants from the PP-E 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 | • All randomized participants who receive at least one dose of IP during the Maintenance Phase of the study (on or after Day 1 visit).<br>• Participants will be assessed according to actual treatment received. | • Safety |
| PK Population | • All participants who receive CAB and / or RPV and undergo PK sampling during the study, and provide evaluable CAB and /or RPV plasma concentration data (i.e. at least 1 non-missing PK assessment (Non-quantifiable [NQ] values will be considered as non-missing values)). | • PK |
| Confirmed Virologic | • Comprised of all participants in the ITT-E | • Genotypic |

| Population | Definition / Criteria | Analyses Evaluated |
|---|---|---|
| Failure (CVF) | population who met Confirmed Virologic Failure (CVF)<br>*CVF during the Maintenance and Extension Phases is defined as: Rebound as indicated by two consecutive plasma HIV-1 RNA levels ≥200 c/mL after prior suppression to <200 c/mL | • Phenotypic<br>• IDMC CVF Analysis |
| All Participants Randomized Population | • All randomized participants | • Secondary population for some analyses |
| Extension Switch Population (ES) | • All randomized subjects from ABC/DTC/3TC arm who receive at least one dose of CAB and/or RPV during the Extension Phase of the study. | • Safety and Efficacy |
| 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 and PK during LTFU |
| Futility analysis population | • Comprised of all participants in the ITT-E population who started study treatment at least 168 days prior to the IDMC cut-off date (in order to account for participants 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

Randomized treatment groups will be displayed as shown in Table 2.

**Table 2 Data Display Treatment Descriptors for Randomized Arms**

| 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 | ABC/DTG/3TC | ABC/DTG/3TC | 2 |

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

- Q4W IM vs. ABC/DTG/3TC

In data displays of Induction Phase data for the All Enrolled Population and Extension Phase data for the Extension Switch population, respectively, study treatment will be displayed as shown in Table 3.

**Table 3 Data Display Treatment Descriptors for All Enrolled Population and Extension Switch Population**

| Data Type | Descriptor |
|---|---|
| Induction Phase Data for All Enrolled Population | Induction Phase ABC/DTG/3TC |
| Extension Phase Data for Extension Switch Population | Switch Q4W IM |

## 5.2. Baseline Definitions

For all assessments evaluated at Screening and/or Week -20 (including labs, vital signs, ECGs, virology assessments, etc.), the Induction Baseline (Week -20) value will be the latest valid (e.g. fasting for lipids) Pre-treatment value observed. This is generally expected to be from the Week -20 visit, although such values may be missing or unscheduled assessments may be performed before treatment start; however, for virology data, this is generally expected to be from the Screening visit (except in the case of CVF for which virology data is expected at Week -20).

Electrocardiograms (ECGs) are to be performed in triplicate on Week -20 visit. The Maintenance Baseline (Week -20) value for an ECG parameter will be the mean of the last pre-treatment set of assessments from the same date.

If pre-treatment genotypic/phenotypic results are available from both the central laboratory and Monogram Biosciences, then Induction Baseline (Week -20)

genotype/phenotype will be determined based only upon the data provided by Monogram assays.

The baseline value for each phase of the study is defined as the last valid (e.g. fasting for lipids) value observed, up to and including date of first dose of study treatment in the respective phase as described in Table 4.

**Table 4 Baseline Definitions for Each Study Phase**

| Definition | Reporting Details |
|---|---|
| Induction Baseline (Week -20) | Last available recorded value up to and including the date of first Induction Phase dose of IP |
| Maintenance Baseline (Day 1) | Last available recorded value up to and including the date of first Maintenance Phase dose of IP |
| Extension Baseline (Week 100) | Last available recorded value up to and including the date of first extension Phase dose of IP<br>• only applicable to ABC/DTG/3TC arm |

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. and secondary efficacy endpoint (HIV-1 RNA <50 c/mL) as described in Section 7.2.5.1. Some countries may be combined for exploratory subgroup analyses with consideration due to the number of participants enrolled.

## 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:<br>• For the proportion of participants with plasma HIV-RNA greater than or equal to 50 c/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 Induction Baseline (Week -20) HIV-1 RNA (<100,000, ≥100,000 c/mL). 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) and repeat analyses of these endpoints at Week 96.<br>See Section 7.1.5 for more 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 participants is small within a particular subgroup, then the subgroup categories may be combined 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 and baseline characteristic factors, will 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 | • Induction Baseline (Week -20) HIV-1 RNA (<100,000, ≥100,000 c/mL)<br>• Gender at birth (Male, Female)<br>For analysis purposes, randomization strata will be derived using eCRF data, even if this differs from the strata captured in RAMOS NG.<br>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:<br>o <35; 35-<50; ≥50 (for statistical modelling analysis, the first two groups will be combined, i.e. <50, ≥50)<br>• Race:<br>o White; Non-White (for statistical modelling analysis)<br>o Black/ African American; Non- Black/ African American<br>• Country (not used for statistical modelling)<br>o Canada;<br>o France;<br>o Germany;<br>o Italy;<br>o Japan<br>o The Netherlands;<br>o Russian Federation;<br>o South Africa;<br>o Spain;<br>o United Kingdom;<br>o United States<br>• Induction Baseline (Week -20) HIV-1 RNA c/mL<br>o <1000;<br>o 1000 to <10,000;<br>o 10,000 to <50,000;<br>o 50,000 to <100,000;<br>o ≥100,000 to <200,000;<br>o ≥ 200,000 c/mL<br>The above subgroup with granular categories for viral load will not be used in statistical modelling. |

| Category | Covariates and / or Subgroups |
|---|---|
| | • Visit of First Suppression (HIV-1 RNA <50 c/mL)[a]:<br>○ Week -20<br>○ Week -16;<br>○ Week -12;<br>○ Week -8;<br>○ Week -4<br>• Maintenance Baseline (Day 1) HIV-1 RNA:<br>○ <50;<br>○ ≥ 50 c/mL.<br>• Induction Baseline (Week -20) CD4+ cell count:<br>○ <200;<br>○ 200 to <350;<br>○ 350 to <500;<br>○ ≥ 500 cells/mm$^3$.<br>• Maintenance Baseline (Day 1) CD4+ cell count:<br>○ <200;<br>○ 200 to <350;<br>○ 350 to <500;<br>○ ≥ 500 cells/mm$^3$.<br>• Derived Maintenance Baseline (Day 1) Centers for Disease Control and Prevention (CDC) category:<br>○ Stage I;<br>○ Stage II;<br>○ Stage III<br>• HIV-1 Subtype at Induction Baseline (Week -20)<br>○ A;<br>○ A1;<br>○ AE;<br>○ AG;<br>○ B;<br>○ C;<br>○ Other<br>• K103N Mutation at Induction Baseline (Week -20):<br>○ Yes vs. No<br>• Induction Baseline (Week -20) BMI (<30, ≥ 30 kg/m^2) |
| **EMA Subgroup Category 3:** | |
| Additional subgroup/covariates for PK/PD efficacy analysis | • Last CAB/RPV Trough (pre-dose) PK concentration by Week 48 (i.e. If pre-dose PK concentration at nominal Week 48 is missing, then last pre-dose PK concentration |

| Category | Covariates and / or Subgroups |
|---|---|
| | prior to Week 48 will be used)<br><br>• Week 8 CAB/RPV Trough PK concentration (i.e. pre-dose PK concentration at nominal visit of Week 8<br><br>The above two covariates will be dichotomized into two subgroup factors as follows:<br>• ≤ first Quartile vs > first quartile;<br>• ≤ Median vs > Median<br>• Needle length for CAB injection at Week 4b: (<2, ≥2 inch);<br>• Needle length for RPV injection at Week 4b: (<2, ≥2 inch);<br>See Section 8.5.1 for additional details regarding attribution of ISRs to causal agent (CAB/RPV) and Needle Length.<br>• Induction Baseline (Week -20) BMI (<30, ≥ 30 kg/m^2) |
| Additional subgroup/covariates for PK/PD safety analysis | • Last CAB/RPV trough PK concentration<br><br>For the plot of "Maximum Change from Maintenance Baseline (Day 1), CBF, 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 the earliest Lab assessment corresponding to the maximum CFB during the Maintenance Phase.<br><br>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 earliest onset date of maximum graded AE (for each preferred term among non-ISR AEs occurring in ≥5% of participants in the Q4W arm during the Maintenance Phase). If a participant does not experience the corresponding preferred term event during the Maintenance Phase, then the last trough value during the Maintenance Phase will be used for the plot. |
| Additional subgroup for Bone Marker analysis | • Induction Baseline (Week -20) BMI (kg/m^2)<br>  ○ <30;<br>  ○ ≥ 30<br>• Smoking status at Screening:<br>  ○ Never;<br>  ○ Current; |

| Category | Covariates and / or Subgroups |
|---|---|
| | ○ Former<br>• Tenofovir (TDF) Use at Maintenance Baseline (Day 1)<br>○ Yes;<br>○ No |
| Additional subgroup for ISR | For each common ISR preferred term (pain, induration, nodules and any other ISR with >=5% subjects for the Q4W arm) during the Maintenance Phase:<br>• Needle Length for Last CAB Injection prior to and including the onset date of the earliest corresponding drug-related CAB ISR with maximum toxicity grade during the Maintenance Phase: (<2, ≥2 inch);<br>• Needle Length for Last RPV Injection prior to and including the onset date of the earliest corresponding drug-related RPV ISR with maximum toxicity grade during the Maintenance Phase: (<2, ≥2 inch);<br>The above subgroup variables will be produce for each common ISR preferred term.<br>Note: If there is no ISR of interest reported during Maintenance Phase for a participant, these subgroup variables will be derived using the needle length of the participant's last injection during Maintenance Phase. |

a) Based on any HIV-1 RNA <50 c/mL within the assessment window defined in Table 13.

## 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 ABC/DTG/3TC if the upper end of a two-sided 95% confidence interval for the difference between the two groups (Q4W IM– ABC/DTC/3TC) 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 ABC/DTC/3TC 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 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. Other Comparisons of Interest

The analysis described above will also be performed using the PP population and the results will be compared for consistency with the results from the ITT-E population.

### 5.5.3. Secondary Comparisons

If the primary comparison of interest (Section 5.5.1) using the ITT-E population demonstrates non-inferiority of Q4W compared to ABC/DTG/3TC then the following key secondary comparisons using the ITT-E population will be tested:

- Treatment with Q4W IM will be declared non-inferior to ABC/DTG/3TC 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 in response rates (Q4W IM– ABC/DTG/3TC) lies above -10%.

- Superiority of Q4W IM compared to ABC/DTG/3TC with respect to change from maintenance baseline (Day 1) HIVTSQs total score at Week 44 using a two-sided 5% level of significance.

- Changes in the PIN acceptance score within the Q4W arm over time using separate two-sided 5% level of significance tests for the change from Week 5 to Week 41 and change from Week 5 to Week 48, respectively.

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 HAT-QoL (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 treatment accountability will be based on GSK Core Data Standards.

Table 5 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 13: List of Data Displays.

**Table 5 Overview of Planned Study Population Analyses**

| Display Type | Data Displays Generated | |
|---|---|---|
| | Table | Listing |
| **Randomisation** | | |
| Randomisation [1] | | Y[2] |
| **Subject Disposition** | | |
| Study Populations [3] | Y | |
| Study Recruitment [3] | Y | |
| Reasons for Screening Failures [3] | Y | Y |
| History of Rescreened Subjects [3] | | |
| Age categories | Y | |
| Subject Disposition | Y[4][5] | |
| Reasons for Withdrawal by Visit | Y[4][5] | 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 [6] | Y | Y |
| Race & Racial Combinations [7] | Y | Y |
| Hepatitis Status at Induction Baseline (Week -20) | Y | |
| CDC Classification of HIV infection (2014) at Maintenance Baseline (Day 1) | Y | |
| Cardiovascular Risk Assessments at Induction Baseline (Week -20) | Y | |
| Distribution of CD4+ Cell Counts at Maintenance Baseline (Day 1) | Y | |

| Display Type | Data Displays Generated | |
|---|---|---|
| | Table | Listing |
| Distribution of Quantitative Plasma HIV-1 RNA and CD4+ Cell Counts at Screening and Induction Baseline (Week -20) | Y | |
| HIV-1 Subtype at Induction Baseline (Week -20) | Y | |
| **Medical Conditions, Concomitant Medications & Antiretroviral Therapy** | | |
| Medical Conditions (Current/Past) [8] | Y | |
| Medical Conditions: Sub-conditions (Current/Past) [9, 10] | Y | |
| Concomitant Medications (non-ART) | Y[10] | |
| Prior Antiretroviral Therapy | | Y |
| Concomitant Antiretroviral Therapy during Induction and Maintenance Phase, respectively | | Y |
| ART Regimen at Randomization | Y | Y |
| Lipid Modifying Agents (Maintenance Baseline (Day 1) and During Maintenance Phase) | Y | |
| Substance use at Screening | Y | |
| Medical History of Seizure | | Y |
| **Other** | | |
| Study Treatment Accountability [11] | | Y |

**NOTES:**

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

1. All Participants Randomized population
2. One listing of participants randomized but not treated, and one listing of planned and actual treatment strata.
3. All Subjects screened population.
4. Participants 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.
5. Analysis of subject disposition will be performed for each study Phase separately, as well as for overall study conclusion.
6. Age and ethnicity collected at Screening; weight and height collected at Baseline (Week -20)
7. The five high level FDA race categories and designated Asian subcategories will be summarised along with all combinations of high level categories which exist in the data. The nine race categories collected will be summarised along with categories for mixed race. A by-subject listing of race will also be produced.
8. Medical conditions will be coded using the Medical Dictionary for Regulatory Activities (MedDRA).
9. Sub conditions are Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, and Nervous System Conditions
10. summarised by, Ingredient combinations
11. Dispensation information (dates and number of tablets dispensed and returned).

# 7. EFFICACY ANALYSES

## 7.1. Primary Efficacy Analyses

### 7.1.1. Endpoint / Variables

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.

### 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 – ABC/DTG/3TC).

### 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 c/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 c/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 c/mL.

### 7.1.5. Statistical Analyses / Methods

Table 6 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 6 Overview of Planned Primary Efficacy Analyses

| Endpoints | Stats Analysis | | | Summary | | Individual | |
|---|---|---|---|---|---|---|---|
| | T | F | L | T | F | F | L |
| **Proportion of Participants with 'HIV-1 ≥ 50 c/mL' at Week 48 – Snapshot** | | | | | | | |
| Primary analysis comparison between the two groups (Q4W IM – ABC/DTG/3TC) in 'HIV-1 RNA≥50 c/mL' 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] | | |
| **Proportion of Participants with 'HIV-1 ≥ 50 c/mL' at Week 96 – Snapshot** | | | | | | | |
| Repeat of the Primary Analysis at Week 96 (see details of efficacy analysis described in Section 7.1) | | | | | | | |

**NOTES:**

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual participant 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 5.4.2).
4. Plot of the difference in proportion of participants with HIV-1 RNA ≥50 c/mL (Snapshot algorithm) and its 95% confidence intervals for 'overall' (on the top of the figure) and by subgroup at Week 48/Week 96.
5. Study outcomes based on the Snapshot algorithm by subgroup at Week 48/Week 96 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 participants 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 c/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 16). In addition, participants who discontinue for reasons not related to adverse event with on-treatment HIV-1 RNA result at the time of discontinuation ≥ 50 c/mL or who change study treatment not permitted per protocol during Maintenance Phase before the analysis visit are classified as 'HIV-RNA ≥ 50 c/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 for Induction Baseline (Week -20) HIV-1 RNA (<100,000, ≥100,000 c/mL) and gender 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 four analysis strata:
  - Induction Baseline (Week -20) HIV-1 RNA < 100 000 c/mL AND Male gender at birth
  - Induction Baseline (Week -20) HIV-1 RNA < 100 000 c/mL AND Female gender at birth
  - Induction Baseline (Week -20) HIV-1 RNA ≥ 100 000 c/mL AND Male gender at birth
  - Induction Baseline (Week -20) HIV-1 RNA ≥ 100 000 c/mL AND Female gender at birth
- If $n_k$ is the number of CAB LA + RPV LA treated participants, $m_k$ is the number of ABC/DTG/3TC control arm treated participants, and $N_k = n_k + m_k$ is the total number of participants in the *k*th stratum, then the CMH estimate is given by

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

where

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

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

**Primary Statistical Analyses**

- 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 RNA $\geq$ 50 c/mL at Week 48 per FDA Snapshot for CAB LA + RPV LA and ABC/DTG/3TC control arm, respectively, for the *kth* stratum.

**Model Results Presentation**

- Adjusted CMH estimate of the difference in the proportion of participants with 'HIV-1 RNA≥50' between each treatment group (CAB LA + RPV LA – ABC/DTG/3TC) 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 participants with 'HIV-1 RNA≥50' in the CAB LA + RPV LA group minus proportion of participants with 'HIV-1 RNA≥50' in the ABC/DTG/3TC 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 fla or fc 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 Subgroups
    - An analysis for demographic and baseline characteristic subgroups listed in Section 5.4.2 will be performed. This will show the proportion of participants 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. The confidence interval will be calculated using an unconditional exact method (Chan, 1999) with two inverted one-sided tests based on the score statistic. These results will also be presented graphically.
    - 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.

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 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 – ABC/DTC/3TC).

### 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 c/mL while the participant is on treatment within the analysis visit window of interest are classified as HIV-1 RNA < 50 c/mL.

### 7.2.5. Statistical Analyses / Methods

Table 7 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 7 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/Week 96 – Snapshot[1]** | | | | | | | |
| Key Secondary Analysis (Week 48) | 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 at Week 48/Week 96 (refer to Section 13.6.4)** | | | | | | | |
| Kaplan-Meier estimate | | | | Y | | | |

| Endpoints | Stats Analysis | | | Summary | | Individual | |
|---|---|---|---|---|---|---|---|
| | T | F | L | T | F | F | L |
| **Proportion of Participants with Plasma HIV-1 RNA ≥ 50 copies/mL over time (Maintenance Phase)– Snapshot** | | | | | | | |
| by Visit | | | | Y | Y[4] | | |
| by Visit and Subgroup[5] | | | | Y | Y[7] | | |
| **Proportion of Participants with Plasma HIV-1 RNA < 50 copies/mL over time (Maintenance Phase)– Snapshot** | | | | | | | |
| by Visit | | | | Y | Y[6] | | |
| by Visit and Subgroup [5] | | | | Y | Y[7] | | |
| **Proportion of Participants with Plasma HIV-1 RNA < 200 copies/mL over time (Maintenance Phase)– Snapshot** | | | | | | | |
| by Visit | | | | Y[8] | Y[9] | | |
| **Proportion of Participants with Plasma HIV-1 RNA ≥ 200 copies/mL over time – Snapshot** | | | | | | | |
| by Visit | | | | Y[8] | Y[9] | | |
| **Proportion of Participants with Plasma HIV-1 RNA < 50 copies/mL at Week 48/Week 96 by delay in IP injection [10] - Snapshot** (exploratory analysis) | | | | | | | |
| by Delay in IP injection | | | | Y | | | |
| **Proportion of Participants with Plasma HIV-1 RNA < 2 copies/mL (exploratory analysis)** | | | | | | | |
| by Visit - Observed Case Analysis | | | | Y[11] | | | |
| **Time from First HIV-1 RNA < 50 copies/mL until Initiation of Maintenance Phase Treatment** | | | | | | | |
| | | | | Y | | | |

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- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual participant observed raw data.

1. This analysis will be performed using the similar approach as described for the primary analysis in Section 7.1
2. Generated using the 'Intent-to-Treat Exposed' (primary) and 'Per-Protocol' (sensitivity) populations.
3. Study outcomes (i.e., 'HIV-1 RNA < 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 participants with HIV-1 RNA ≥50c/mL 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 5.4.2)
6. Line plots, with 95% confidence intervals, for the proportion of participants with HIV-1 RNA<50c/mL by treatment group at each visit. The 95% CIs will be calculated using Exact (Clopper-Pearson) confidence interval if the proportion is 100%; otherwise, they are derived using the normal approximation.
7. Plot of the unadjusted treatment difference and its 95% confidence intervals (Snapshot algorithm) overall and by subgroup at Week 48.
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 participants with HIV-1 RNA <200c/mL and ≥200 c/mL by treatment group at each visit. The 95% CIs will be calculated using Exact (Clopper-Pearson) confidence interval if the proportion is 0% or 100%; otherwise, they are derived using the normal approximation
10. Delay in IP injection (days) is defined in Section 13.6.4
11. Using observed case (OC) data which contains the data that is available at a particular time point, with no imputation for missing values and expanded ± 6-week window for W48/W96 and last value in window (see Section 13.6.4).

## Table 8 Overview of Additional Secondary Efficacy Analyses

| Endpoints | Absolute | | | | | | | Change from Maintenance 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[8] | | Y[2] | Y[3] | | | | | | | |
| Detected vs Non-detected by Visit [1,5] | | | | Y | | | Y[6] | | | | | | | |
| **Confirmed Virologic Failure (CVF)** | | | | | | | | | | | | | | |
| CVF Overall | | | | Y | | | | | | | | | | |
| 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[7] | | | | | | | Y[7] | | | |
| CD8+ observed | | | | Y[7] | | | | | | | Y[7] | | | |
| CD4+/CD8+ ratio observed | | | | Y[7] | | | | | | | | | | |
| **HIV-1 Conditions and Disease Progression** | | | | | | | | | | | | | | |
| HIV Conditions including/excluding Recurrences as recorded in eCRF | | | | Y | | | Y | | | | | | | |
| HIV Disease Progressions [4] | | | | Y | | | | | | | | | | |

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- 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 participant 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 and expanded ± 6 week window for W48/W96 and last value in window (see Section 13.6.4).
2. Individual plasma HIV-1 RNA only for participants who are in the category of 'viral load ≥50 c/mL' at Week 48 per Snapshot algorithm or who are CVF participants. The figures will display all HIV-1 RNA values collected.

3. For CVF participants (during the Induction and Maintenance Phase, respectively, and participants with viral load ≥ 50 c/mL at any time during the Maintenance Phase).
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. Using observed case (OC) data which contains the data that is available at a particular time point, with no imputation for missing values
8. Using log10 transformed values

#### 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 Snapshot HIV-1 RNA <50 c/mL replacing Snapshot HIV-1 ≥ 50 c/mL |
| **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 IM – ABC/DTG/3TC) and corresponding 95% confidence interval.<br>• Non-inferiority will be concluded if the lower bound of the two-sided 95% confidence interval for the CMH adjusted treatment difference (Q4W IM – ABC/DTG/3TC) is greater than -10%. |
| **Subgroup Analyses** |
| • Treatment Heterogeneity across randomization strata:<br>o As specified in Section 7.1.5.1 but with Snapshot HIV-1 RNA <50 c/mL replacing Snapshot HIV-1 RNA ≥ 50 c/mL. |
| **Sensitivity and Supportive Analyses** |
| 1. Per-protocol population analysis:<br>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, 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, emergent chemistry/haematology abnormality, participants with hepatobiliary abnormality criteria.

## 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. Adverse Events of Special Interest Analyses

A comprehensive list of MedDRA terms based on clinical review will be used to identify Anxiety, Depression and Suicidality/Self-Injury Adverse Events of Special Interest (AESI). [Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting and/or emerging data from on-going studies may highlight additional adverse events of special interest, therefore the list of terms to be used for each event of interest and the specific events of interest will be based on the safety review team (SRT) agreements in place at the time of reporting.] The details of the planned grouping and planned displays are provided in Section 13.6.3 and Appendix 13: List of Data Displays.

## 8.3. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Hematology 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.

## 8.4. 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 > 550ms.

## 8.5. Planned Safety Analysis

Table 9 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 13: List of Data Displays.

## Table 9 Overview of Planned Safety Analyses

| Endpoint | Absolute | | | | Change from Maintenance Baseline | | | | Max Post Maintenance 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 Schedule [1] | Y | | | | | | | | | | | |
| **Injection Needle** | | | | | | | | | | | | |
| Length and Gauge | Y | | | | | | | | | | | |
| **Adverse Events[3]** | | | | | | | | | | | | |
| All AEs by SOC | Y | | | | | | | | | | | |
| All AEs by SOC and Toxicity[3] | Y[24] | | | 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[24] | | | | | | | | | | | |
| 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[24] | | | Y | | | | | | | | |
| Common Non-Serious AEs (FDAAA) | Y | | | | | | | | | | | |
| Number of occurrences of Common Non-serious AEs by SOC (EudraCT) | Y | | | | | | | | | | | |
| Number of occurrences of SAEs, Fatal SAEs, and Drug-related SAEs | Y | | | | | | | | | | | |

| Endpoint | Absolute | | | | Change from Maintenance Baseline | | | | Max Post Maintenance BL | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Summary | | Individual | | Summary | | Individual | | Summary | | Individual | |
| | T | F | F | L | T | F | F | L | T | F | F | L |
| (EudraCT) | | | | | | | | | | | | |
| Cumulative AEs by visit | Y | | | | | | | | | | | |
| Depression, Suicidal and Self-Injury AEs by Prior History | Y[25] | | | | | | | | | | | |
| **Suicidality assessment** | | | | | | | | | | | | |
| PSRAE | | | | Y[7] | | | | | | | | |
| Columbia suicidality (C-SSR) | Y | | | | | | | | | | | |
| **Injection Site Reaction Adverse Events** [12] | | | | | | | | | | | | |
| ISR AEs (Event-Level) [17] | Y | | | | | | | | | | | |
| ISR AEs (Subject-Level) [18] | Y | Y | | | | | | | | | | |
| ISR AEs (Subject-Level) by Visit and Severity | Y | Y[19] | | | | | | | | | | |
| Maximum ISR AE Grade by Needle Length [21] | Y | | | | | | | | | | | |
| **Laboratory: Chemistry and Hematology** | | | | | | | | | | | | |
| Clinical Chemistry & Renal Biomarkers [11] | Y | | | | Y | | | | Y [23] | | | |
| %Lipids[22] | | | | | Y | | | | | | | |
| NCEP shifts in lipids | | Y | | | | | | | Y | | | |
| Hematology | Y | | | | Y | | | | Y[23] | | | |
| **Laboratory: Urinalysis (regardless of fasting status)** | | | | | | | | | | | | |
| Urine Dipstick | Y[8] | | | | | | | | | | | |
| Urine Concentration & Renal biomarkers[12] | | | | | Y | | | | | | | |
| **Laboratory: Hepatobiliary** | | | | | | | | | | | | |
| Liver Assessment | | | | Y [14] | | | | | | | | |
| Hepatobiliary Abnormality criteria | Y[15] | | | Y | | | | | | | | |
| Liver Chemistries | | | | Y[16] | | | | | | Y[9] | | |
| **Laboratory: Markers** | | | | | | | | | | | | |
| Bone markers | | | | | Y[10] | | | | | | | |
| **ECG** | | | | | | | | | | | | |
| ECG findings | Y | | | Y | | | | | | | | |

| Endpoint | Absolute | | | | Change from Maintenance Baseline | | | | Max Post Maintenance BL | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Summary | | Individual | | Summary | | Individual | | Summary | | Individual | |
| | T | F | F | L | T | F | F | L | T | F | F | L |
| ECG values | | | | | Y | | | | | | | |
| QTC values by Category | Y | | | | Y | | | | Y | | | |
| **Other** | | | | | | | | | | | | |
| Vital Signs | | | | | Y | | | | | | | |
| Weight & BMI | | | | | Y[24] | | | | | | | |
| Abacavir HSR | | | | Y[13] | | | | | | | | |
| Participants who became Pregnant | | | | Y | | | | | | | | |
| Patient Profiles | | | | Y[20] | | | | | | | | |

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

1. Refer to Section 13.6.2 for defining Extent of Exposure and adherence to Q4W dosing intervals,
2. Includes reason for any dose change/interruption.
3. For AEs reported more than once by a participant, the most severe intensity will be included. Separate summary tables including and excluding injection site adverse reactions.
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. ABC/DTG/3TC.
7. Four PSRAE listings: Event and Description (Section 1 and Section 2), Possible Cause (Section 3), Section 4 and Section 5 - Section 8.
8. Shift table summarising Maintenance Baseline (Day 1) vs. maximum Maintenance Phase result for urine dipstick protein.
9. Scatter plot of baseline vs. maximum post-baseline for ALT. Scatter plot of maximum ALT vs. maximum Bilirubin. Matrix plot of maximum liver chemistries.
10. Bone markers including: Bone-specific alkaline phosphatase, procollagen type 1 N-propeptide, type 1 collagen cross-linked C-telopeptide, osteocalcin, 25 hydroxy-Vitamin D.
11. Renal markers: 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
12. Repeat for CAB/RPV, CAB, RPV respectively.
13. Separate listings for exposure to abacavir, history of drug allergies, family conditions, skin rash, symptoms, vital signs, individual symptoms and diagnostic category assignment.
14. Separate listings for time of event, RUCAM score, biopsy, imaging, past/ current conditions and follow up
15. One summary of subjects and another table showing Subject Ids. Table of subjects meeting hepatobiliary abnormally criteria during the maintenance oral lead-in Phase will also be produced.
16. Patient profiles for participants meeting protocol defined liver stopping criteria and for patients with virologic failure. Patient profiles can also be provided for any other participants, as necessary for medical review.
17. Event-level summary: Percentages based on total number of ISR events within each treatment group including distribution of grade, duration, and event characteristics;
18. Subject-Level summary: Characteristics of ISR AE (Overall and by Common ISRs); Percentage based on number of participants 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;
19. A corresponding plot of all grades and a separate plot of grade 3-5 events will be produced
20. Patient profiles are not planned. But it can be produced post hoc, as necessary.
21. Please refer to Section 5.4.2 "Additional subgroup for ISR" for derivation of needle length used in this summary

22. Please refer to Section 13.6.3 for defining percentage change from Maintenance Baseline (Day 1) in Lipids
23. Separate tables will be produced for Maintenance Phase data and Oral Lead-in period data (see Table 25 and Table 26)
24. Change from Induction Baseline (Week -20) for BMI and Weight.
25. By SOC and Maximum Toxicity, and history based on prior/current medical conditions collected at Screening

### 8.5.1. Injection Site Reactions

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), or drug-related associated to CAB and/or RPV.

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.

ISRs will be attributed to the needle length 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 needle length in those events where both drugs are given on one side and their needle lengths are different, then the attribution to a needle length will remain unknown.

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

### 8.5.2. Statistical Analyses/Methods

| **Statistical Analyses** |
|---|
| **Endpoints** |
| • Change from Maintenance Baseline (Day 1) in Bone Markers at Week 48 |
| **Covariates** |
| • Treatment (Q4W IM, ABC/DTG/3TC)<br>• Induction Baseline (Week -20) HIV-1 RNA (<100,000, ≥100,000 c/mL), Gender at Birth, TDF use at Maintenance Baseline (Day 1), Age, body mass index category at Induction Baseline (Week -20), smoking status, and Log-transformed bone marker value at Maintenance Baseline (Day 1) (as defined 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 Maintenance baseline (i.e. log of ratio of post-baseline value over Maintenance baseline value) for each bone marker will be analysed for the comparison between the two treatment arms.<br>• Analysis of covariance (ANCOVA) model will be used with the above covariates/subgroups. Age and Log-transformed bone marker value at Maintenance Baseline (Day 1) will be included as continuous variables in the model and all other covariates will be included as categorical variables. |
| **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 Maintenance Baseline (Day 1) value rather than the change in the log ratio. The change in the ratio can then be translated into percent change from maintenance baseline (Day 1) (e.g. the ratio $bb_{48}/bb_{bl}$ = 1.3 can be translated into 30% increase from baseline).<br>• For each treatment, adjusted (geometric) means of ratio and corresponding confidence intervals will be presented. Adjusted point estimates will be derived as LSMEAN S using the observed margins (OM) option within PROC MIXED in SAS.<br>• The adjusted (geometric mean) difference of the ratio (post-baseline value)/(baseline value) between the two treatments with the corresponding confidence interval and *p*-value will be presented<br>• Interactions between treatment and each of the covariates will be investigated but not included in the main model. If interactions are found to be significant (p-value <0.10), results will be presented separately by subgroup. |
| **NOTES:**<br>• Statistical analysis will only be performed when all expected data through Week 48 has been received from the laboratory. |

# 9. PHARMACOKINETIC AND PHARMACOKINETIC/PHARMACODYNAMIC 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

#### 9.1.1.1. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 13.5.3 Reporting Standards for Pharmacokinetic)

#### 9.1.1.2. Derived Pharmacokinetic Parameters

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

### 9.1.2. Planned Analyses

Table 10 provides an overview of the planned analyses based on observed plasma CAB/RPV concentration data only with full details being presented in Section Appendix 13: List of Data Displays.

Unless otherwise specified, drug concentration and pharmacodynamic measures will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

**Table 10 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 concentrations by Snapshot virologic Response | | | | Y | Y | | |
| Analysis of Snapshot 'HIV-1 RNA≥50' at Week 48 by last trough CAB/RPV concentration, Week 8 trough concentration, and subgroup [6] – Univariable analysis /multivariable analysis | Y | | | | | | |
| Individual CAB/RPV Concentration-Time Profiles for Participants with HIV-1 RNA ≥ 50 c/mL at Week 48 | | | | | Y | | |
| Change from Maintenance Baseline (Day 1) in 2hr post-dose QTc and 2-hour post-dose CAB & RPV concentration at Week 4b, Week 48 | | | | | | Y | |
| Maximum Change from Maintenance Baseline (Day 1) in ALT/Total Bilirubin versus Last Trough CAB/RPV Concentrations | | | | | | Y | |
| Maximum Toxicity Grades of Most Frequently Reported AEs versus Last Trough CAB/RPV PK Concentrations | | | | | | Y | |

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- 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 participant 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 ) and not affected by dosing errors or oral bridging.
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 5.4.2. i.e. randomisation strata, baseline and demographic factors, and additional subgroups for PK/PD analyses

### 9.1.3. Statistical Analyses/Methods

| **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 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 is 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 (or W96) |
| **Covariates** |
| • Randomisation strata, demographic and baseline characteristics, and additional subgroup/covariates for PK/PD efficacy analysis (i.e. last CAB/RPV trough concentration and CAB/RPV trough concentration at the nominal Week 8 visit, Induction Baseline (Week -20) BMI, needle length for CAB/RPV injections at Week 4b)— see derivation details 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/subgroups. This logistic regression analysis will be performed for each covariate, separately (univariable analysis), and will also be performed with one multivariable analysis using Backward stepwise selection approach to identify the covariates potentially affecting virologic response. |
| **Model Checking & Diagnostics** |
| • For the multivariable 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 univariable analysis) will be determined using the backward stepwise selecting approach. The last trough and Week 8 trough PK concentration will be logarithmically transformed with base of 2 (i.e. one-unit increase of the point estimate of log2 PK concentration is equivalent to 'doubling the concentration' in the original value). 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 when all remaining covariates have p-value <15%.<br>• If problems with model convergence occur due to zero event counts or complete/quasi-complete separation, then alternative methods such as exact logistic regression may be used. |
| **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 PK concentration. |

# 10. HEALTH OUTCOMES ANALYSES

## 10.1. Endpoint / Variables

- Change from Maintenance Baseline (Day 1) in total "treatment satisfaction" score, and individual item scores of the HIV Treatment Satisfaction Status Questionnaire (HIVTSQs);
- Change in treatment satisfaction over time (using the HIVTSQc change version) at Week 48;
- Change from Week 5 in Dimension Scores and proportion of participants considering pain and local reactions following injection using PIN (Perception of iNjection Questionnaire) (Q4W arm only);
- Change from Maintenance Baseline (Day 1) in Subscale of Life satisfaction, HIV medication, and disclosure worries using HAT-QoL;
- Change from Maintenance Baseline (Day 1) in Total Score, Mental health component (MCS) and physical component summary (PCS) using SF-12;
- Change from Maintenance Baseline (Day 1) in treatment acceptance using ACCEPT;
- Change from Week 4b in tolerability of injections using NRS (Q4W arm only)

### 10.1.1. Summary Measure

Mean treatment difference (Q4W IM – ABC/DTG/3TC) at visits of interest through to Week 96 (i.e. the assessment visits detailed in Table 11), excluding PIN and NRS endpoints.

Mean change at visits of interest through to Week 96 (i.e. the assessment visits detailed in Table 11), for PIN and NRS endpoints.

### 10.1.2. Population of Interest

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

### 10.1.3. 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 27 for definition of on-treatment), the data will be computed or imputed (see Section 13.6.6).

### 10.1.4. Planned Health Outcomes Analyses

Table 11 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 11 Overview of Planned Health Outcome Analyses

| Endpoints | Absolute | | | | | | | Change from Maintenance 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, withdrawal (Q4W arm only) | | | | | | | | | | | | | | |
| Individual Item Scores | | | | Y | | | | | | | | | | |
| Domain of 'Bother from injection site reactions', 'Leg movement', 'Sleep', 'Acceptability' | Y[4] | | | Y | | | | | | | Y[5] | | | |
| **Health-related quality of life (HATQoL)** at Day 1, Week 24, 48, 96, withdrawal | | | | | | | | | | | | | | |
| Individual Item Scores | | | | Y | | | | | | | | | | |
| Subscale of Life satisfaction, HIV medication, and disclosure worries | | | | Y | | | | Y | Y[1] | | Y | | | |
| **Health Status (SF-12) at** Day 1, Week 24, 48, 96, Withdrawal | | | | | | | | | | | | | | |
| Individual Item Scores | | | | Y | | | | | | | | | | |
| Total Score, Mental health component (MCS) and physical component summary (PCS)[2] | | | | Y | | | | Y | Y[1] | | Y | | | |
| **Treatment Satisfaction Score (HIVTSQs)** at Day 1, Week 4b, 24, 44, 96, withdrawal | | | | | | | | | | | | | | |
| Individual Item Scores | | | | Y | | | | | | | | | | |
| Individual Item Scores by Subgroup[3] | | | | Y | | | | | | | | | | |
| Treatment Satisfaction Score | Y | | | Y | | | | Y | Y[1] | | Y | | | |
| **Treatment Satisfaction Score Change (HIVTSQc)** at Week 48, withdrawal | | | | | | | | | | | | | | |
| Individual Item Scores | | | | Y | | | | | | | | | | |
| Treatment Satisfaction Score Change | Y | | | Y | | | | | | | | | | |

| Endpoints | Absolute | | | | | | | Change from Maintenance 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 Day 1, Week 8, 24, 48, 96, withdrawal | | | | | | | | | | | | | | |
| Proportion of Individual item score | | | | Y | | | | | | | | | | |
| Acceptance/General Dimension Score | | | | Y | | | | Y | Y[1] | | Y | | | |
| **Tolerability of injection (NRS)** at Week 4b, 5, 40, 41, 96 (Q4W arm only) | | | | | | | | | | | | | | |
| Proportion of Individual item score | | | | Y | | | | | | | | | | |
| Tolerability Score (Q4W IM only) | | | | Y | | | | | | | Y | | | |
| **Treatment Preference** at Week 48 (Q4W arm only) | | | | | | | | | | | | | | |
| Treatment: Monthly injection vs Daily oral ART | | | | Y | | | | | | | | | | |

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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. Subgroups: Induction Baseline (Week -20) HIV-1 RNA (<100,000, ≥100,000 c/mL), gender at birth, age (<35; 35-<50; ≥50), Maintenance Baseline (Day 1) CD4+ cell count ( <200; 200 to <350; 350 to <500; ≥ 500 cells/mm3), and race (i.e. white, non-white).
4. Statistical analysis (i.e. p-value) produced only for the acceptance score comparing Week 40/41/96 to Week 5.
5. Change versus Week 5 for PIN.

### 10.1.5. Statistical Analyses/Methods

| Statistical Analyses |
|---|
| **Endpoints** |
| • Change from Maintenance Baseline (Day 1) in<br>  • HIVTSQs total treatment satisfaction score 24, 44, and 96<br>  • ACCEPT general acceptance score at Week 8, 24, 48, and 96<br>  • SF-12: Total Score, physical component summary(PCS) and mental component summary(MCS) at week 24, 48, and 96<br>  • HATQoL (Life satisfaction, HIV medications, disclosure worries) at Week 24, 48, and 96. |
| **Model Specification** |
| • An analysis of covariance (ANCOVA) model will be used at each visit at Maintenance Phase with covariates: treatment, age (<50, ≥ 50 years old), Induction Baseline (Week -20) HIV-1 RNA (<100,000, ≥100,000 c/mL), gender at birth, race (i.e. white, non-white) and Maintenance Baseline (Day 1) score value (as a continuous variable).<br>• Adjusted point estimates will be derived as LSMEANS using the observed margins (OM) option within PROC MIXED in SAS.<br>• No adjustment for multiplicity will be applied as these analyses will be considered supportive.<br>• 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 (p<0.10), results may be presented separately by subgroup. |
| **Dataset** |
| • LOCF dataset will be used. |
| **Model Results Presentation** |
| • Adjusted treatment difference (Q4W IM – ABC/DTG/3TC), its 95% CI and the associated p-value. The interaction between treatment and the baseline score will be included in a footnote.<br>• Plots of adjusted mean change from Maintenance Baseline (Day 1) (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), Induction Baseline (Week -20) HIV-1 RNA (<100,000 c/mL, ≥ 100,000 c/mL), Gender at birth, and Race (white, non-white)<br>• Adjusted point estimates will be derived as LSMEANS using the observed margins (OM) option within PROC MIXED in SAS.<br>• 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. If interactions are found to be significant (p<0.10), results may be presented separately by subgroup.<br>• No adjustment for multiplicity will be applied as these analyses will be considered supportive. |
| **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 – ABC/DTG/3TC). |
| **Statistical Analyses** |
| **PIN** |
| • Change from Week 5 in the PIN acceptance score at Week 41 and Week 48 (Q4W arm only) |
| **Statistical Test** |
| • The Wilcoxon Signed-Rank Test will be used to evaluable whether the change from Week 5 to Week 41 and to Week 48, respectively, is statistically different than zero based on a two-sided p<0.05. Separate tests will be performed for the change from Week 5 to Week 41 and for the change from Week 5 to Week 48. |
| **Dataset** |
| • LOCF dataset will be used |
| **Results Presentation** |
| • Summary statistics at each timepoint (Week 5, Week 41 and W48) and p-value for each comparison (W48/W41) versus scores at Week 5 |

# 11. VIROLOGY

The virology analyses will be for the CVF populations using genotype and phenotype data based on population sequencing assay, unless otherwise specified.

Table 12 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 13: List of Data Displays.

**Table 12 Overview of Planned Virology Analyses**

| Endpoint | Absolute | | | |
|---|---|---|---|---|
| | Summary | | Individual | |
| | T | F | F | L |
| **Genotypic resistance** at time of CVF[1] | | | | |
| Prevalence of Resistance Mutations | Y [2] | | | Y [4] |
| Prevalence of Emergent Resistance Mutations – Relative to Genotype at Baseline (Week -20) [5] | Y [2] | | | |
| **Phenotypic resistance** at time of CVF[1] | | | | |
| Prevalence of Phenotype | Y [3] | | | Y [4] |
| Fold Change for CAB, RPV, DTG | Y | | | |
| Change from Induction Baseline (Week -20) in Fold Change to CAB, RPV, DTG. | Y | | | |
| IN, PR/RT Replication Capacity | | | | Y |
| **Other** | | | | |
| Viral load, Genotypic and Phenotypic data for Participants with genotype and/or phenotype data for CVF and non-CVF participants | | | | Y [4] |
| Prevalence of Resistance Mutations at Induction Baseline (Week -20) | Y [2] | | | |

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- Individual = Represents FL related to any displays of individual participant 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 participant 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 participants with IN resistance mutations or major mutations in the classes of NNRTI, NRTI, PI, respectively, as defined in 13.6.7
3. Separate outputs by phenotypic cut-off and by number of drugs to which participants are resistant.
4. Includes the following at all available timepoints (including screening, Week -20, and all post-baseline samples): HIV-1 subtype (Induction Baseline (Week -20)), resistance mutations and fold change to EFV/ETR/RPV, DTG/RAL/EVG/CAB and ARTs (for the ABC/DTG/3TC arm) received during the Maintenance Phase. Non-CVF participants may include those with genotype/phenotype data upon withdrawal from treatment with last on-

treatment HIV-1 RNA ≥200 c/mL.

5. Emergent Mutations defined in Section 13.6.7

Additional analyses for HIV-1 resistance may be carried out on peripheral blood mononuclear cell (PBMC) samples collected at Day 1 and Week 96 (or withdrawal if prior to Week 96).

If pre-treatment genotypic/phenotypic results are available from both the central laboratory and Monogram Biosciences, then Baseline genotype/phenotype will be determined based only upon the data provided by Monogram assays.

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# 13. APPENDICES

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| Section 13.5 | Appendix 5: Data Display Standards & Handling Conventions |
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# 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 the Per Protocol population are those deviations which may

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

The following criteria define the protocol deviations which, if they occur prior to an analysis timepoint of interest (e.g. Week 48/96), will lead to exclusion of a participant 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 participant 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 | Participant deviates from inclusion or exclusion criteria that may significantly affect exposure, response to therapy or participant 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 | Participant 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) up to an analysis timepoint of interest (i.e. Week 48/96), meeting the following conditions:<br><br>Maintenance Phase:<br>1. Maintenance Phase Week 48 analysis only:<br>• 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 visit of interest; or<br>2. Week 96 analysis only:<br>• For participants discontinuing injections by Week 52: 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 visit of interest.<br>• For participants receiving injections beyond Week 52: Three 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 visit of interest; or<br>3. At least 10% of total time on-treatment with under dosing deviations in the Maintenance Phase up to the analysis visit of interest (i.e. Week 48/96), where the |

| Number | Exclusion Description |
|---|---|
| | % with non-compliance is derived the ratio of the total number of non-compliant under dosing days occurring as of the date of the last analysis timepoint snapshot viral load (i.e. last on-treatment viral load during the Maintenance Phase up to Study Day 378 for W48 and up to Study Day 714 for W96) divided by the number of days on-treatment from start of Maintenance Phase treatment to the date of the last analysis timepoint snapshot viral load, and non-compliance days are defined as follows:<br><br>**ABC/DTG/3TC Arm:**<br>a. Duration of interruptions in ABC/DTG/3TC arm ART for reasons other than treatment-related adverse events/laboratory abnormalities (based on Exposure eCRF forms);<br><br>**Q4W IM Arm:**<br>a. Length of time (in days) until next injection from date of dosage/administration deviation potentially resulting in under dosage (e.g. 1ml administered instead of 2ml)<br>b. Length of time (in days) in excess beyond 35 days between injections post Week 12 and in excess beyond 28 days for Week 8 and Week 12 (e.g. missed or late injection visit)<br>c. Length of time (in days) in excess beyond 35 days from last injection until start of oral bridging post Week 12 and exceeding 4 weeks for Week 8 and Week 12 |
| 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 participant 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). |

## 13.2. Appendix 2: Schedule of Activities

### 13.2.1. Protocol Defined Schedule of Events

| Procedures | Screening [a] | Induction Phase by Week | | | | | Maintenance Phase by Week | | | | | | | | | | | | | | | | Extension Phase by Week | | | | | | Withdrawal[y] | Long-Term Follow-Up |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Baseline (-20) | (-16) | (-12, -8) | (-4) | WD[y] | Day 1 | 4a | 4b – LA arm | 5[t] – LA arm | 8, 12, 16, 20 | 24 | 28, 32, 36 | 40, 44 | 41 – LA arm | 48 | 52 - LA Arm | 56 | 60 – LA Arm | 64, 72, 80, 88 | 68,76, 84, 92 - LA Arm | 96 | 100 | 104a | 104b – Switch Arm | 108 | 112, 116, 120,124 ABC/DTG/3TC Switch Arm | Q4W after 108 (LA arm) or after 124 (Switch Arm) | Q12W beginning 112 (LA Arm) or 124 (Switch Arm)[j] | | |
| **Clinical and Other Assessments** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Written Informed Consent | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eligibility Verification (Inclusion / Exclusion Criteria) | X | X | | | X [b] | | | | | | | | | | | | | | | | | X [b] | | | | | | | | |
| Randomization | | | | | | | X | | | | | | | | | | | | | | | | | | | | | | | |
| Demography | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Medical History[c] | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Medication History / Prior ART History | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

| Procedures | Screening [a] | Induction Phase by Week | | | | | Maintenance Phase by Week | | | | | | | | | | | | | | | | Extension Phase by Week | | | | | | Withdrawal [y] | Long-Term Follow-Up |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Baseline (-20) | (-16) | (-12, -8) | (-4) | WD [y] | Day 1 | 4a | 4b – LA arm | 5 [t] – LA arm | 8, 12, 16, 20 | 24 | 28, 32, 36 | 40, 44 | 41 – LA arm | 48 | 52 - LA Arm | 56 | 60 – LA Arm | 64, 72, 80, 88 | 68,76, 84, 92 - LA Arm | 96 | 100 | 104a | 104b – Switch Arm | 108 | 112, 116, 120,124 ABC/DTG/3TC Switch Arm | Q4W after 108 (LA arm) or after 124 (Switch Arm) | Q12W beginning 112 (LA Arm) or 124 (Switch Arm) [j] | | |
| Symptom Directed Physical Exam and Medical Assessment [d] | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Weight, BMI, and Height [e] | | X | | | | X | | | | | | | | | | X | | | | | | X | | | X | | | | X | |
| Cardiovascular Risk Assessment | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Vital Signs (BP, HR, temperature) [f] | X | X | | | | X | X | | | | | | | | | X | | | | | | X | | | X | | | | X | |
| 12-Lead ECG [g] | X | X pre-dose x3 | | | | X | X | | X [g] | | | | | | | X [g] | | | | | | X | | | X | | | | X | |
| CDC 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 | X | X | X | X | X | X | X | X |

| Procedures | Screening [a] | Induction Phase by Week | | | | | Maintenance Phase by Week | | | | | | | | | | | | | | | | Extension Phase by Week | | | | | | Withdrawal [y] | Long-Term Follow-Up |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Baseline (-20) | (-16) | (-12, -8) | (-4) | WD [y] | Day 1 | 4a | 4b – LA arm | 5 [t] – LA arm | 8, 12, 16, 20 | 24 | 28, 32, 36 | 40, 44 | 41 – LA arm | 48 | 52 - LA Arm | 56 | 60 – LA Arm | 64, 72, 80, 88 | 68,76, 84, 92 - LA Arm | 96 | 100 | 104a | 104b – Switch Arm | 108 | 112, 116, 120,124 ABC/DTG/3TC Switch Arm | Q4W after 108 (LA arm) or after 124 (Switch Arm) | Q12W beginning 112 (LA Arm) or 124 (Switch Arm) [j] | | |
| AE and SAE Assessment, Con Meds | X [h] | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| ISR Assessment (LA Arm Only) | | | | | | | | | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X<br>If appli-cable |
| Columbia Suicide Severity Rating Scale (eC-SSRS) [i] | X | X | | | X | X | X | | X | | X | X | X | X | | X | | | X | W 7 2 | W84 | X | | | | | | | X | |
| Clinical Chemistry and Hematology | X | X | X | X | X | X | X | X | | | X | X | X | X | | X | X | X | X | X | | X | | X | | X | X | | X | X | X |
| Rapid Plasma Reagin (RPR) | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Pregnancy Testing [j] | S | U | S | S | S | S | U | S | U | | S | S | S | S | | S | S | S | S | S | S | S | S | S | U | S | S | S - Q4W | | S | S |
| HIV-1 RNA and sample for storage [k] | X [k] | X | X | X | X | X | X | | X | | X | X | X | X | | X | S [k] | X | X | X | | X | S [k] | | X | X | X | | X | X | X |

| Procedures | Screening [a] | Induction Phase by Week | | | | | Maintenance Phase by Week | | | | | | | | | | | | | | | | Extension Phase by Week | | | | | | Withdrawal [y] | Long-Term Follow-Up |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Baseline (-20) | (-16) | (-12, -8) | (-4) | WD [y] | Day 1 | 4a | 4b – LA arm | 5 [t] – LA arm | 8, 12, 16, 20 | 24 | 28, 32, 36 | 40, 44 | 41 – LA arm | 48 | 52 - LA Arm | 56 | 60 – LA Arm | 64, 72, 80, 88 | 68,76, 84, 92 - LA Arm | 96 | 100 | 104a | 104b – Switch Arm | 108 | 112, 116, 120,124 ABC/DTG/3TC Switch Arm | Q4W after 108 (LA arm) or after 124 (Switch Arm) | Q12W beginning 112 (LA Arm) or 124 (Switch Arm) [j] | | |
| CD4+ | X | X | X | X | X | X | X | | X | | X | X | X | X | | X | | X | X | X | | X | | | X | X | X | | X | X | X |
| CD8+ | | X | | | X | | X | | X | | | X | | | | X | | | | | | X | | | X | | | | | X | |
| Urinalysis [l] | | X | | | | | X | X | | | | X | | | | X | | | | | | X | | | X | | | | | X | |
| Fasting Lab Assessments: Glucose, Cholesterol (Total, HDL and LDL) and Triglycerides [m] | | X | | | | | X | | | | | | | | | X | | | | | | X | | | | | | | | X | |
| Hepatitis B (HBsAg), Anti-HBc, and Anti-HBsAG<br><br>Hepatitis C (anti-HCV Ab) | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| *HLA-B*5701* | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| PT/PTT/INR | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

| Procedures | Screening [a] | Induction Phase by Week | | | | | Maintenance Phase by Week | | | | | | | | | | | | | | | | Extension Phase by Week | | | | | | Withdrawal [y] | Long-Term Follow-Up |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Baseline (-20) | (-16) | (-12, -8) | (-4) | WD [y] | Day 1 | 4a | 4b – LA arm | 5 [t] – LA arm | 8, 12, 16, 20 | 24 | 28, 32, 36 | 40, 44 | 41 – LA arm | 48 | 52 - LA Arm | 56 | 60 – LA Arm | 64, 72, 80, 88 | 68,76, 84, 92 - LA Arm | 96 | 100 | 104a | 104b – Switch Arm | 108 | 112, 116, 120,124 ABC/DTG/3TC Switch Arm | Q4W after 108 (LA arm) or after 124 (Switch Arm) | Q12W beginning 112 (LA Arm) or 124 (Switch Arm) [j] | | |
| Renal and Bone marker analytes (blood/urine) [n] | | | | | | | X | | | | | | | | | X | | | | | | X | | | | | | | X | |
| Peripheral Blood Mononuclear Cells (PBMCs) [o] | | | | | | | X | | | | | | | | | | | | | | | X | | | | | | | X | |
| Genetic Sample [p] | | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

| Procedures | Screening [a] | Induction Phase by Week | | | | | Maintenance Phase by Week | | | | | | | | | | | | | | | Extension Phase by Week | | | | | | Withdrawal [y] | Long-Term Follow-Up |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Baseline (-20) | (-16) | (-12, -8) | (-4) | WD [y] | Day 1 | 4a | 4b – LA arm | 5 [t] – LA arm | 8, 12, 16, 20 | 24 | 28, 32, 36 | 40, 44 | 41 – LA arm | 48 | 52 - LA Arm | 56 | 60 – LA Arm | 64, 72, 80, 88 | 68,76, 84, 92 - LA Arm | 96 | 100 | 104a | 104b – Switch Arm | 108 | 112, 116, 120,124 ABC/DTG/3TC Switch Arm | Q4W after 108 (LA arm) or after 124 (Switch Arm) | Q12W beginning 112 (LA Arm) or 124 (Switch Arm) [j] | | |
| **Pharmacokinetics (CAB + RPV only)** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| PK Sample (S)= Storage sample | | | | | | | | | X v w | X t v | X | X | X | X | X v | X v | X | X | X | S | | X v | X | | X v w | X | | | | X | S |
| **Investigational Products** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Oral CAB and Oral RPV Dispensation | | | | | | | X | X | | | | | | | | | | | | | | | X x | X x | | | | | | | | |
| ABC/DTG/3TC Dispensation (or DTG alternate) | | X | X | X | X q r | | X | X | | | X | X | X | X | | X | | X | | X | | X | | | | | | | | | |
| Study Treatment Accountability (pill counts) | | | X | X | X r | X | X | X | X u | | X | X | X | X | | X | | X | | X | | X | X | X | X u | | | | | | |
| IM Study Treatment Administration – Q4W throughout Maintenance and Extension Phase | | | | | | | | | X | | X | X | X | X | | X | X | X | X | X | X | X | X | X | X s | X | X | X – cont dosing Q4W | | | |

| Procedures | Screening [a] | Induction Phase by Week | | | | | Maintenance Phase by Week | | | | | | | | | | | | | | | | Extension Phase by Week | | | | | | Withdrawal [y] | Long-Term Follow-Up |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Baseline (-20) | (-16) | (-12, -8) | (-4) | WD [y] | Day 1 | 4a | 4b – LA arm | 5 [t] – LA arm | 8, 12, 16, 20 | 24 | 28, 32, 36 | 40, 44 | 41 – LA arm | 48 | 52 - LA Arm | 56 | 60 – LA Arm | 64, 72, 80, 88 | 68,76, 84, 92 - LA Arm | 96 | 100 | 104a | 104b – Switch Arm | 108 | 112, 116, 120,124 ABC/DTG/3TC Switch Arm | Q4W after 108 (LA arm) or after 124 (Switch Arm) | Q12W beginning 112 (LA Arm) or 124 (Switch Arm) [j] | | |
| **Patient Reported Outcomes [z]** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| HAT-QoL (short form) | | | | | | | X | | | | | X | | | | X | | | | | | X | | | | | | | X | |
| SF-12 | | | | | | | X | | | | | X | | | | X | | | | | | X | | | | | | | X | |
| ACCEPT | | | | | | | X | | | | W 8 | X | | | | X | | | | | | X | | | | | | | X | |
| HIVTSQ(s) | | | | | | | X | | X | | | X | | W 44 | | | | | | | | X | | | | | | | X | |
| HIVTSQ(c) | | | | | | | | | | | | | | | | X | | | | | | | | | | | | | X | |
| PIN (LA Arm Only)[aa] | | | | | | | | | | X | | | | | X | X | | | | | | X | | | | | | | X | |
| NRS (LA Arm Only) | | | | | | | | | X | X | | | | W 40 | X | | | | | | | X | | | | | | | | |
| Preference (LA Arm Only) | | | | | | | | | | | | | | | | X | | | | | | | | | | | | | | |
| Follow Up Visit: Conduct ~4 weeks after the last dose of IP. Required only if the participant has ongoing AEs / 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 Induction Phase as soon as all Screening assessments are complete. Participants may be rescreened once and will be assigned a new participant number.
b. Confirmation of eligibility to enter the Maintenance Phase, eligibility to enter the Extension Phase.
c. 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 and neurologic disorders.
d. 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 participant management and / or care.
e. Height collected at Baseline only.
f. Measure vital signs after about 5 minutes of rest in a semi-supine position.
g. A 12-lead ECG will be performed after resting in a semi-supine position for at least 5 minutes. Perform ECG at Baseline (Week [-20]) in triplicate prior to dosing. For participants randomized to CAB LA + RPV LA, at Week 4b and Week 48, a second ECG will be obtained approximately 2 hours after the last injection and just prior to the 2 hour post dose PK sampling.
h. Collect SAEs at Screen only if associated to study participation.
i. On Day 1, the eC-SSRS is to be administered prior to randomization. During the Maintenance Phase, the eC-SSRS will be administered at each Q4W visit through the Week 48 primary endpoint, and then followed by Q12W assessments thereafter through Week 96 (Week 60, 72, 84, 96). Preferably completed at the beginning of the visit following administration of other patient reported questionnaires required prior to injections.
j. Conduct pregnancy tests for only women of childbearing potential at every visit throughout the study, including Q4W during the Extension Phase. Remind females of reproductive potential of the need to avoid pregnancy while in study and adherence to the study's contraception requirements. A negative urine pregnancy test is required prior to beginning the Induction Phase (Week [-20]), on Day 1 (preferably prior to randomization), and at Week 4b (or Week 104b for participants transitioning from ABC/DTG/3TC) prior to the first injection. Serum pregnancy test can substitute for urine pregnancy test if locally required, but must be appropriately timed to confirm pregnancy status prior to e.g randomization and first IM administration. S=Serum/U=Urine.
k. Plasma for storage will be used: to determine genotypic eligibility at Screen, for possible future analyses, as back- up in case samples are lost or damaged in transit to the lab and for genotypic and phenotypic analyses in cases of virologic failure. 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.
l. A morning specimen is preferred. To assess biomarkers: urine albumin/creatinine ratio; urine protein/creatinine ratio; and urine phosphate.
m. Overnight fast is preferred; however, a minimum of a 6 hour fast is acceptable.
n. 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
o. Whole blood/Peripheral Blood Mononuclear Cell collection samples may be used for virologic analyses. PBMCs will be collected at Day 1, Week 96, Withdrawal visits.
p. Informed consent for genetic research must be obtained before sample collection. Sample may be collected at any visit after signing informed consent, but preferably at the Week [-20] visit.
q. Instruct participants to continue to take the ABC/DTG/3TC regimen until Day 1 of the Maintenance Phase. Participants will be randomized at Day 1 to continue on ABC/DTG/3TC arm or begin oral CAB + oral RPV. Day 1 dosing should occur after randomization to determine defined treatment for the Maintenance Phase.
r. Remind participants of the potential change in study treatment and visit frequency beginning at Day 1.
s. Visit Week 104b is only required for participants transitioning from the ABC/DTG/3TC arm.
t. The Week 5 visit should be performed approximately 7 days after the first injections at Week 4b (3 to 10 day window allowed).

u. For oral CAB + RPV only.
v. Take PK samples pre-dose. Week 4b (and Week 104b for participants transitioning to LA from ABC/DTG/3TC) PK sample should be taken after review of the PK diary and prior to the final oral CAB + RPV dose. A second sample will be taken at Week 4b, Week 48, and Week 96 (and Week 104b), approximately 2 hours post-injections. The Week 5 and Week 41 visit can be performed at any time from 3 to 10 days after the Week 4b and Week 40 injection, respectively. PK samples at Week 5 and Week 41 can be taken at any time during the visit.
w. Participants should take the last dose of oral CAB+RPV at Week 4b (and Week 104b for participants transitioning to LA from ABC/DTG/3TC) in the clinic after PK sampling and injections should be administered within 2 hours of this where possible.
x. For participants transitioning to CAB LA + RPV LA from ABC/DTG/3TC only.
y. Follow Up Visit: Conduct approximately 4 weeks after the last dose of oral 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.
z. With the exception of the NRS questionnaire, patient reported questionnaire/surveys are recommended to be administered at the beginning of the visit before any other clinical assessments are conducted, and prior to completion of the eCSSRs assessments. Only conduct questionnaires/surveys at Withdrawal if occurring prior to Week 96 (The NRS will not be collected at Withdrawal).
aa. The PIN, Preference, and NRS questionnaires are to be administered only to participants receiving CAB LA + RPV LA injections. The NRS should be collected 30 to 60 minutes post-injection (and at Week 5 and Week 41, one week post-injections) - the participant should record the maximum level of pain experienced with the most recent injections.

Note: BMI- Body mass Index, 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

Laboratory data, vital signs, ECGs, NRS questionnaire (health outcomes) assessments, protocol deviations, 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, induction, 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.

Induction Phase and Maintenance Phase assessments are assigned based on the Induction Phase Study Day and Maintenance Phase Study Day, respectively, as shown in Table 13 and Table 14. The analysis visits from Week 4 to Week 100 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 participants continuing Q4W IM dosing into the Extension Phase, and based on the Extension Phase Study Day for participants switching from the control arm to Q4W IM dosing for the Extension Phase as shown in in Table 15. The analysis visits from Week 104 (except for Follow-up) in the Extension Phase should be only applied to the assessments that are already assigned to Extension Phase (on-treatment).

Assessment windows at key analysis time points for the snapshot efficacy data are shown in Table 16.

Long-term Follow-up Phase assessments are assigned based on the LTFU study day as shown in Table 17. See Section 13.6.1 for derivation of Induction, Maintenance, Extension and LTFU Study Day.

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

### Table 13 Assessment Windows for Screening and Induction Phase Data

| Analysis Set / Domain | Parameter | Target Study Day | Analysis Window | Analysis Timepoint |
|---|---|---|---|---|
| All | All | The day of earliest record | Induction Study Day ≤1 | Screening |
| | | 1 | Last available recorded value up to and including the date of first Induction Phase dose of IP | Induction Baseline (Week -20) |
| | | 29 | 2 ≤ Induction Study Day ≤ 42 | Week -16 |
| | | 57 | 43 ≤ Induction Study Day ≤ 70 | Week -12 |
| | | 85 | 71 ≤ Induction Study Day ≤ 98 | Week -8 |
| | | 113 | 99 ≤ Induction Study Day ≤ 126 | Week -4 |
| | | 141 | 127 ≤ Induction Study Day ≤ Induction ART Stop Day[a] + 1 | Day 1 |
| | | | **For Participants not continuing into Maintenance Phase:**<br><br>Induction Study Day > (Induction ART Stop Day[a] +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.

a. ABC/DTG/3TC stop day: the last permanently stop day among all ARTs taken during Induction Phase.

## Table 14 Assessment Windows Maintenance Phase Data

| All Parameters expect where noted [f] | Analysis Window | Target Study Day | Analysis Timepoint |
|---|---|---|---|
| | | | |
| | | | |
| | Last available recorded value up to and including the date of first Maintenance Phase dose of IP | 1 | Maintenance Baseline (Day 1) |
| 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 |
| 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 [c], Renal and Bone marker analytes [d], Lipids [e], Weight, Height, Vital Signs | 323 ≤ Study Day ≤ 378 | 337 | Week 48 |
| | 323 ≤ Study Day ≤ 350 | | |
| | 351 ≤ Study Day ≤ 378 | 365 | Week 52 |
| | 379 ≤ Study Day ≤ 406 | 393 | Week 56 |
| | 407 ≤ Study Day ≤ 434 | 421 | Week 60 |
| | 435 ≤ Study Day ≤ 476 | 449 | Week 64 |
| | 477 ≤ Study Day ≤ 532 | 505 | Week 72 |
| | 533 ≤ Study Day ≤ 588 | 561 | Week 80 |
| | 589 ≤ Study Day ≤ 644 | 617 | Week 88 |
| ECG, CD8, CD4/CD8 ratio, Urinalysis [c], Renal and Bone marker analytes [d], Lipids [e], Weight, Height, Vital Signs | 645 ≤ Study Day ≤ 714 | 673 | Week 96 |
| | 645 ≤ Study Day ≤ 686 | | |
| ECG, CD8, CD4/CD8 ratio, Urinalysis [c], Renal and Bone marker analytes [d], Lipids [e], Weight, Height, Vital Signs | For 'ABC/DTG/3TC' arm:<br><br>715 ≤ Study Day ≤ Maintenance ABC/DTG/3TCStop Day[b] + 1<br><br>For 'Q4W' arm:<br>715 ≤ Study Day ≤ Max (Day of Last Q4W IM Dose + 35, Last Oral dose Day + 1) [a] | 701 | Week 100 |

| All Parameters expect where noted [f] | Analysis Window | Target Study Day | Analysis Timepoint |
|---|---|---|---|
| | For 'ABC/DTG/3TC' arm:<br><br>687 ≤ Study Day ≤ Maintenance ABC/DTG/3TCStop Day[b] + 1<br><br>For 'Q4W' arm:<br>687 ≤ Study Day ≤ Max (Day of Last Q4W IM Dose + 35, Last Oral dose Day + 1) [a] | 701 | Week 100 |
| | For participants who discontinued from oral lead-in during Maintenance Phase, Study Day > (Day of last oral lead-in dose+1)<br><br>Participants discontinued from ABC/DTG/3TC' and not continuing into extension Phase<br>Study Day > (Maintenance ABC/DTG/3TC Stop Day[b] +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).

a. Last Q4W IM / last oral dose is only applied to participants who permanently discontinue from study treatment

b. ABC/DTG/3TCstop day: the last permanently stop day among all ARTs taken during Maintenance Phase.

c. **Urinalysis**: All parameters provided by the central laboratory under the category of urinalysis, including 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.

d. **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.

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

f. Analysis windows for parameters with sparse collection are noted.

## Table 15 Assessment Windows for Extension Phase Data

| All Parameters expect where noted [b] | Analysis Window | Target Extension Phase Study Day | Target Study Day | Analysis Timepoint |
|---|---|---|---|---|
| **Participants Continuing Randomized Q4W IM Regimen** | | | | |
| Urinalysis [c] | Study day of Nominal Week 100 visit < Study Day ≤ 770 | | 729 | Week 104 |
| | Study day of Nominal Week 100 visit < Study Day ≤ 742 | | | |
| | 743≤ Study Day ≤770 | | 757 | Week 108 |
| | 771≤ Study Day ≤882 | | 841 | Week 120 |
| | (7*w - 41) ≤ Study Day ≤ (7*w + 42) | | 7*w + 1 | Week w w = 132, 144,… |
| **Participants Switching to Q4W IM Dosing** | | | | |
| | Last available recorded value up to and including the date of first Extension Phase dose of IP | 1 | | Extension Baseline (W100) |
| ECG, CD8, CD4/CD8 ratio, Urinalysis [a], Weight, Vital Signs | 2 ≤ Extension Study Day ≤ 70 | 29 | | Week 104 |
| | 2 ≤ Extension Study Day ≤ 42 | | | |
| | 43 ≤ Extension Study Day ≤ 70 | 57 | | Week 108 |
| | 71 ≤ Extension Study Day ≤ 98 | 85 | | Week 112 |
| | 99 ≤ Extension Study Day ≤ 126 | 113 | | Week 116 |
| | 127 ≤ Extension Study Day ≤ 154 | 141 | | Week 120 |
| | 155 ≤ Extension Study Day ≤ 182 | 169 | | Week 124 |
| | 183 ≤ Extension Study Day ≤ 266 | 253 | | Week 136 |
| | (7*(w-100) - 41) ≤ Study Day ≤ (7*(w-100) + 42) | 7*(w-100) + 1 | | Week w w = 148, 160,… |
| | For participants 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 100 visit is the original visit from eCRF (i.e. the VISIT variable as opposed to AVISIT)

a. **Urinalysis**: All parameters provided by the central laboratory under the category of urinalysis, including 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.

b. Analysis windows for parameters with sparse collection are noted.

## Table 16 Assessment Windows for Summary of Snapshot Data — Data assigned to Maintenance Phase Only

| Snapshot Analysis Windows (if no viral load data in default window, expand upper bound to + 6 weeks) | | Analysis Timepoint |
|---|---|---|
| **Default (midpoint between planned visits) [a]** | **Expanded +6 Week upper window** | |
| Last available recorded value up to and including the date of first Maintenance Phase dose of IP | Last available recorded value up to and including the date of first Maintenance Phase dose of IP | Maintenance Baseline (Day 1) |
| 2 ≤ Study Day ≤ 42 | 2 ≤ Study Day ≤ 70 | Week 4 |
| 43 ≤ Study Day ≤ 70 | 43 ≤ Study Day ≤ 98 | Week 8 |
| 71 ≤ Study Day ≤ 98 | 71 ≤ Study Day ≤ 126 | Week 12 |
| 99 ≤ Study Day ≤ 126 | 99 ≤ Study Day ≤ 154 | Week 16 |
| 127 ≤ Study Day ≤ 154 | 127 ≤ Study Day ≤ 182 | Week 20 |
| 155 ≤ Study Day ≤ 182 | 155 ≤ Study Day ≤ 210 | Week 24 |
| 183 ≤ Study Day ≤ 210 | 183 ≤ Study Day ≤ 238 | Week 28 |
| 211 ≤ Study Day ≤ 238 | 211 ≤ Study Day ≤ 266 | Week 32 |
| 239 ≤ Study Day ≤ 266 | 239 ≤ Study Day ≤ 294 | Week 36 |
| 267 ≤ Study Day ≤ 294 | 267 ≤ Study Day ≤ 322 | Week 40 |
| 295 ≤ Study Day ≤ 322 | 295 ≤ Study Day ≤ 350 | Week 44 |
| 295 ≤ Study Day ≤ 378 | 295 ≤ Study Day ≤ 378 | Week 48 |
| 365 ≤ Study Day ≤ 406 | 365 ≤ Study Day ≤ 434 | Week 56 |
| 407 ≤ Study Day ≤ 434 | 407 ≤ Study Day ≤ 462 | Week 60 |
| 435 ≤ Study Day ≤ 476 | 435 ≤ Study Day ≤ 490 | Week 64 |
| 477 ≤ Study Day ≤ 532 | 477 ≤ Study Day ≤ 546 | Week 72 |
| 533 ≤ Study Day ≤ 588 | 533 ≤ Study Day ≤ 602 | Week 80 |
| 589 ≤ Study Day ≤ 644 | 589 ≤ Study Day ≤ 658 | Week 88 |
| 631 ≤ Study Day ≤ 714 | 631 ≤ Study Day ≤ 714 | Week 96 |

**NOTES:**
Apply Snapshot analysis windows only to viral load data that is on-treatment (per Table 27) within the Maintenance Phase (Per Table 22)

a. ± 6 Week window always used at key analysis timepoints (Week 48 and Week 96)

**Table 17 Assessment Windows for Summaries of Long-Term Follow Up Phase Data for Participants 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<br>m = 15, 18, 21,… | 7*m |
| **NOTES:**<br>• An assessment may be slotted to both LTFU and Maintenance /Extension Phase | | |

### 13.3.3. Assessment Window for Study Conclusion

The study conclusion and Phase conclusion records in disposition data will be slotted based on Table 13 (for Induction Phase conclusion records), Table 14 (for Maintenance Phase conclusion records) and Table 15 (for extension Phase conclusion records). However, if the discontinuation date is post-treatment (based on Table 27), then the discontinuation will be slotted to the participants the last attained on-treatment analysis visit across all assessments (e.g. analysis visit corresponding to the last on-treatment lab assessment), 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 18.

**Table 18 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 4B |
| | | 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 | |
| | | 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 + 672 | Date of 1st Injection + 630 < Assessment Date ≤ Date of 1st Injection + 714 | Week 96 |
| Note: Apply NRS analysis windows only to assessments that are on-treatment (per Table 27) within the Maintenance Phase (Per Table 22) | | | | |

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

PIN, HATQoL, SF-12, HIVTSQs, HIVTSQc, ACCEPT, and Treatment Preference questionnaire assessments will be assigned to analysis visits as follows:

1. Maintenance Baseline (Day 1) will be defined as last available recorded value up to and including the date of first Maintenance Phase dose of study treatment (expected to be collected at Day 1).
2. If the nominal visit identifier as captured in the source dataset corresponds to a scheduled collection per the Time and Events Schedule (see Section 13.2 and
3. Table 19) and the assessment is collected in the Maintenance Phase (per Table 22), then the nominal visit identifier will be kept as the analysis visit (excluding Day 1 which will normally be assigned to Maintenance Baseline (Day 1).
4. If the nominal visit identifier is unscheduled or withdrawal, then the following procedure will be used:
    a) Assign the assessment to a study Phase according to Table 22. Proceed to step b if the assessment is assigned to the Maintenance Phase.
    b) Identify the 'last nominal visit' with the HO assessment performed prior to the unscheduled/withdrawal visit to be slotted.
    c) The unscheduled/withdrawal visit will be slotted to the planned nominal visit subsequent to the 'last nominal visit'. If the 'last nominal visits' does

not exist (e.g. no records originate from a planned nominal visit), then the unscheduled/withdrawal visit will be slot to the first planned nominal visit after Day 1.

Example 1, for HATQoL, the planned nominal visits are Week 24, 48, and 96. If a participant 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—see Section 13.3.6.

**Table 19 Planned Nominal Visit of Health Outcome Data**

| Endpoints | Day1 | W4b | W5 | W8 | W24 | W40 | W41 | W44 | W48 | W52 | W96 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| PIN (Q4W) | | | x | | | | x | | x | | x |
| HATQoL | x | | | | x | | | | x | | x |
| SF-12 | x | | | | x | | | | x | | x |
| HIVTSQs | x | x (Q4W arm only) | | | x | | | x | | | x |
| HIVTSQc | | | | | | | | | x | | |
| ACCEPT | x | | | x | x | | | | x | | x |
| NRS (Q4W) | | x | x | | | x | x | | | | x |
| Treatment preference (Q4W) | | | | | | | | | x | | |

### 13.3.4.3. Evaluable Criteria for Observed Case Displays — NRS and PIN

Post the visit slotting as described above, data that is assessed outside of 5-9 days post injection (relative to date of injection at Week 4b/40, respectively) 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 (at Week 4b/40, respectively) are received will be excluded from Observed Case Displays (see Table 20). However, these data will still be used for LOCF displays.

**Table 20 Evaluable Time Windows for Observed Cases Summary Tables**

| Endpoints | W4b | W5 | W40 | W41 |
|---|---|---|---|---|
| PIN (Q4W) | | Within Day 5-9 post W4b injection | | Within Day 5-9 post W40 injection |
| NRS (Q4W) | On the same Day of W4b injection | Within Day 5-9 post W4b injection | On the same day of W40 injection | Within Day 5-9 post W40 injection |

### 13.3.5. Assessment Window for PK concentration Data

For PK concentration data at nominal withdrawal/unscheduled/LTFU Month1 visits during Maintenance or Extension Phase (after assignment to study Phase according to Table 22), the visit will be slotting to the analysis visit per the following steps:

- Identify the 'last nominal PK visit' with the PK 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 earliest nominal visit from the following:
    - nominal visit corresponding to the next planned pre-dose PK assessment visit (excluding timepoints with storage PK collection), that is subsequent to the 'last nominal PK visit' during the same study Phase.
    - nominal visit of the next planned injection visit within the study phase occurring on or after the date of the PK assessment

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, 56, 60, 96, 100, 108 for the Q4W arm; and a Week 104b, 108 for the ABC/DTG/3TC arm. Planned Injection visits are Week 4, Week 8, continuing every 4 weeks for the Q4W arm and every 4 weeks for the ABC/DTG/3TC arm starting at W104.

Example 1: If a participant has the 'last nominal PK visit' at Week 24 and then withdraws (around Week 28) with a Maintenance Phase PK assessment labelled as 'LTFU Month 1' Phase, this assessment will be slotted to the subsequent planned PK assessment visit of Week 28.

Example 2: If a participant has the 'last nominal PK visit' at Week 60 and then withdraws (around Week 88, with last injection at W84) with a Maintenance Phase PK assessment labelled as 'LTFU Month 1', then this assessment will be slotted the subsequent planned injection visit of Week 88 (next injection visit). 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 NRS questionnaire Health Outcomes assessments:

1. the assessment closest to the window target Study Day will be used;
2. if there are multiple assessments equidistant from the target Day, then the earliest assessment will be used.

For other Health outcome assessments (i.e. apart from NRS) and PK concentration data, the following hierarchy will be used to determine the value to be used for summary statistics of observed values:

1. if there are multiple on-treatment assessments assigned to the same analysis visit, the assessment from the original planned nominal visit will be used for summary statistics.
2. If there are multiple on-treatment assessments assigned to the same analysis visit and none originate from a planned nominal visit (e.g. two unscheduled/withdrawal nominal visits), then
    a. the assessment closest to the window target Study Day will be used;
    b. if there are multiple assessments equidistant from the target Study Day, 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, all applicable assessments, irrespective of proximity to the target study day, will be used when categorizing values across visits, such as ‘maximum grade’ or ‘at any time’, 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 21. 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/ AIDS-defining conditions, health outcomes assessments, vital signs, and ECGs will be assigned to study Phases as defined as in Table 22. 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 21 Assignment of Study Phases for AEs**

| Study Phase | Date range |
|---|---|
| Screen | Date < Induction Treatment Start Date |
| Induction | **For participants continuing into Maintenance Phase:**<br><br>Induction Treatment Start Date ≤ Date < Maintenance Treatment Start Date<br><br>**For participants not continuing into Maintenance Phase:**<br><br>Date ≥Induction Treatment Start Date |
| Maintenance | **DTG/ABC/3TC Arm:**<br>**For participants continuing into Extension Phase:**<br>Maintenance Treatment Start Date ≤ Date < Start Date of Extension Phase with Oral lead-in of CAB + RPV (expected to be WK100)<br><br>**For participants not continuing into Extension Phase:**<br><br>Date ≥Maintenance Treatment Start Date |
| | **Q4W IM Arm:**<br><br>**For participants continuing into Extension Phase:**<br><br>Maintenance Treatment Start Date ≤ **Date** < Date of Nominal Week 100 Visit<br><br>**For participants not continuing into Extension Phase:**<br><br>Maintenance Treatment Start Date ≤ **Date** < LTFU ART Start Date |
| Extension | **Participants Switching from Maintenance DTG/ABC/3TC Arm to Q4W:**<br><br>Start Date of Extension Phase Oral lead-in of CAB + RPV ≤ **Date** < LTFU ART Start Date<br><br>**Participants continuing maintenance Q4W into Extension Phase**<br><br>Date of Nominal Week 100 Visit ≤ **Date** < LTFU ART Start Date |

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

**Table 22 Assignment of Study Phases for Lab assessments, ECG, Vital Sign, PK, Health Outcomes, PDs, and HIV associated/AIDS-defining conditions**

| Study Phase | Date range |
|---|---|
| Screen | Date ≤ Induction Treatment Start Date |
| Induction | **For participants continuing into Maintenance Phase:**<br><br>Induction Treatment Start Date < Date ≤ Maintenance Treatment Start Date<br><br>**For participants not continuing into Maintenance Phase:**<br><br>Date > Induction Treatment Start Date |
| Maintenance | **DTG/ABC/3TC Arm:**<br><br>**For participants continuing into Extension Phase:**<br>Maintenance Treatment Start Date < Date ≤ Start Date of Extension Phase Oral lead in of CAB + RPV (expected to be nominal Week 100)<br><br>**For participants <u>not</u> continuing into Extension Phase:**<br>Date >Maintenance Treatment Start Date |
| | **Q4W IM Arm:**<br><br>**For participants continuing into Extension Phase:**<br>Maintenance Treatment Start Date < **Date** ≤ Date of Nominal Week 100 visit<br><br>**For participants <u>not</u> continuing into Extension Phase:**<br>Maintenance Treatment Start Date < **Date** ≤ LTFU ART Start Date |
| Extension | **Participants Switching from Maintenance DTG/ABC/3TC Arm to Q4W IM:**<br>Start Date of Extension Phase Oral lead-in of CAB + RPV < **Date** ≤ LTFU ART Start Date<br><br>**Participants continuing maintenance Q4W IM into Extension Phase**<br>Date of Nominal Week 100 Visit < **Date** ≤ LTFU ART Start Date |

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

**Table 23 Assignment of Study Phases for Concomitant medication/ART**

| Concomitant during: | Date range |
|---|---|
| Prior | **Medication Taken** < Induction Treatment Start Date |
| Induction | **For participants continuing into Maintenance Phase:**<br><br>Induction Treatment Start Date ≤ **Medication Taken** < Maintenance Treatment Start Date<br><br>**For participants not continuing into Maintenance Phase:**<br><br>**Medication Taken** ≥ Induction Treatment Start Date<br><br>*Note: ART stopped on the start date of Induction Treatment will be considered Prior ART and will not be considered concomitant during the Induction Phase.* |
| Maintenance | **DTG/ABC/3TC Arm:**<br>**For participants continuing into Extension Phase:**<br>Maintenance Treatment Start Date ≤ **Medication Taken** < Start Date of Extension Phase with Oral lead-in of CAB + RPV (expected to be WK100)<br><br>**For participants not continuing into Extension Phase:**<br><br>**Medication Taken** ≥ Maintenance Treatment Start Date<br><br>*Note: ART stopped on the start date of Maintenance Treatment will be considered concomitant during the Induction Phase and will not be considered concomitant during the Maintenance Phase.* |
| | **Q4W IM Arms:**<br><br>**For participants continuing into Extension Phase:**<br>Maintenance Treatment Start Date ≤ **Medication Taken** < Date of Nominal Week 100 visit<br><br>**For participants <u>not</u> continuing into Extension Phase:**<br>Maintenance Treatment Start Date ≤ **Medication Taken** < LTFU ART Start Date<br><br>*Note: ART stopped on the start date of Maintenance Treatment be considered concomitant during the Induction Phase and will not be considered concomitant during the Maintenance Phase.* |

| Concomitant during: | Date range |
|---|---|
| Extension | **Participants Switching from Maintenance DTG/ABC/3TC Arm to Q4W IM:**<br><br>Start Date of Extension Phase Oral lead-in of CAB + RPV ≤ **Medication Taken** < LTFU ART Start Date<br><br>*Note: ART stopped on the start date of Extension Phase Oral lead-in of CAB + RPV will not be assigned to the Extension Phase.*<br><br>**Participants continuing maintenance Q4W IM into Extension Phase**<br>Date of Nominal Week 100 Visit ≤ **Medication Taken** < LTFU ART Start Date<br><br>*Note: ART taken stopped on the date of nominal Week 100 visit will be considered concomitant during the Maintenance Phase and will not be considered concomitant during the Extension Phase.* |
| Long-Term Follow-Up | **For participants who received at least one CAB and/or RPV Injection:**<br><br>**Medication Taken** ≥ LTFU ART Start Date |

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 24 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) |

- D**ate** = 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 participant 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.

#### 13.4.1.1. Study Periods

Certain displays will be produced for data collected during the oral-lead-in and during the first 52 weeks of the Maintenance Phase, respectively. These period variables are defined in Table 25 and Table 26 and will be reflected in the datasets in separate variables.

**Table 25 Assignment of Study Period for AE Data**

| Study Period | Date range |
|---|---|
| Maintenance up to Week 52 | **ABC/DTG/3TC Arm:**<br><br>**For participants continuing beyond Week 52:**<br>Maintenance Treatment Start Date ≤ **Date** < Date of Study Day 378 (Upper Assessment Window for Week 52)<br><br>**For participants <u>not</u> continuing beyond Week 52:**<br>Date ≥ Maintenance Treatment Start Date |
| | **Q4W IM Arm:**<br><br>**For participants continuing beyond Week 52:**<br>Maintenance Treatment Start Date ≤ **Date** < Date of Study Day 378 (Upper Assessment Window for Week 52)<br><br>**For participants <u>not</u> continuing beyond Week 52:**<br>Maintenance Treatment Start Date ≤ **Date** < LTFU ART Start Date |
| Oral lead-in | **Q4W IM Arm:**<br><br>**For participants receiving at least one Maintenance Phase Injection:**<br>Maintenance Treatment Start Date ≤ **Date** < Date of First IM injection<br><br>**For participants withdrawing prior to first Maintenance Phase Injection:**<br>Date ≥ Maintenance Treatment Start Date |

**Table 26 Assignment of Study Period for Lab assessments:**

| Period | Date range |
|---|---|
| Maintenance<br>up to Week 52<br>[Note: this is derived for LAB assessments only] | **ABC/DTG/3TC Arm:**<br><br>**For participants continuing beyond Week 52:**<br>Maintenance Treatment Start Date < **Date** ≤ Date of Study Day 378 (Upper Assessment Window for Week 52)<br><br>**For participants <u>not</u> continuing beyond Week 52:**<br>Date >Maintenance Treatment Start Date |
| | **Q4W IM Arm:**<br><br>**For participants continuing beyond Week 52:**<br>Maintenance Treatment Start Date < **Date** ≤ Date of Study Day 378 (Upper Assessment Window for Week 52)<br><br>**For participants <u>not</u> continuing beyond Week 52:**<br>Maintenance Treatment Start Date < **Date** ≤ LTFU ART Start Date |
| Oral lead-in<br>[Note: this is derived for LAB assessments only] | **Q4W IM Arm:**<br><br>**For participants receiving at least one Maintenance Phase Injection:**<br><br>Maintenance Treatment Start Date < **Date** ≤ Date of First IM injection<br><br>**For participants withdrawing prior to first Maintenance Phase Injection:**<br><br>Date >Maintenance Treatment Start Date |

### 13.4.2. Treatment State

Within each treatment study Phase (i.e. Induction, 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 27 will be considered 'on-treatment' for the given Phase.

**Table 27 Treatment State within Study Phases**

| Study Phase[a] | Treatment State | Date Range |
|---|---|---|
| Screen | Pre-treatment | All assessments/events within Phase |
| Induction | On-treatment | Date ≤ Induction Treatment Stop Date + 1 |
| | Post-treatment | Date > Induction Treatment Stop Date + 1 |
| Maintenance | On-treatment | ABC/DTG/3TC ART arm:<br>Date ≤ Maintenance ART Stop Date + 1 |
| | | IM Q4W arm:<br><br>Date ≤ max (Date of Last Q4W IM Dose + 35, Last Oral Dose Date + 1) |
| | Post-treatment | ABC/DTG/3TC arm:<br>Date > ABC/DTG/3TC Stop Date + 1 |
| | | IM Q4W arm:<br>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 / Induction Treatment stop date is only applied to participants 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 27 will be considered 'on-treatment' for the given Phase. The onset date will be derived based on Table 28.

**Table 28 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<br>If Treatment Start Date ≤ AE Onset Date = AE Onset Date - Treatment Start Date +1<br>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 Induction, 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\mid201584\primary_01 |
| QC Spreadsheet | : \ARWORK\GSK1265744\mid201584\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).<br>• 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):<br>  • 4.03 to 4.23: General Principles<br>  • 5.01 to 5.08: Principles Related to Data Listings<br>  • 6.01 to 6.11: Principles Related to Summary Tables<br>  • 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.<br>• Numeric data will be reported at the precision collected on the eCRF.<br>• 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:<br>  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.<br>  • 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.<br>• Reporting for Data Listings:<br>  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1).<br>  • Unscheduled or unplanned readings will be presented within the subject listings displays. |

| Unscheduled Visits | |
|---|---|
| • Unscheduled visits will be assigned to a study visit using the all-inclusive windows defined in Section 13.3.2.<br>• However, data summaries will only report visits that are planned assessment time points for each parameter (according to the Time and Events table).<br>• 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

| Pharmacokinetic Concentration Data | |
|---|---|
| Descriptive Summary Statistics, Graphical Displays and Listings | Refer to IDSL PK Display Standards.<br>Refer to IDSL Statistical Principle 6.06.1.<br><br>NQ concentration values will be assigned a numeric value equal to the low limit of quantification (LLQ) (Refer to GUI_51487 for further details) for descriptive summary statistics/analysis and summarized graphical displays only.<br><br>Geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and between geometric coefficient of variation (CVb (%)) will be reported.<br>○ $CV_b$ (%) = $\sqrt{}$ (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:<br>o the assessment closest to the window target Study Day;<br>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<br>• 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 by Phase as follows:<br>Induction Phase<br>• Start date of DTG regimen entered onto the Induction Phase IP exposure CRF<br>Maintenance Phase<br>• For participants randomised to Q4W IM, maintenance treatment start date is the date of oral lead-in of CAB+RPV entered onto the Maintenance Phase IP exposure CRF<br>• For participants randomised to ABC/DTG/3TC, maintenance treatment start is DTG regimen start date entered onto the Maintenance Phase IP exposure CRF<br>•<br>Extension Phase<br>• For participants randomised to Q4W IM, extension treatment start date is the date of Nominal Week 100 injection date.<br>For participants randomised to ABC/DTG/3TC, extension treatment start date is the start date of oral lead-in of CAB+RPV entered onto the Extension Phase IP exposure CRF. |

**Induction Phase Study Day**

The Induction Phase Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated/AIDS-defining condition) will be derived as the number of days between the date of the event and the initial start date of DTG in the Induction Phase as follows:

if date of event ≥ start date of Induction Phase DTG, then

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

if date of event < start date of Induction Phase DTG, then

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

if date of event > start date of Maintenance Phase DTG, then

Induction Phase Study Day will not be derived (i.e. will be set to missing).

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

**Study Day**

The Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated/AIDS-defining 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

- Study Day = Date of Event – Start Date of Maintenance Phase IP + 1

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

- Study Day = Date of Event – Start Date of Maintenance Phase IP

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/AIDS-defining 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:<br><br>if date of event ≥ start date of extension Phase IP, then<br><br>$\text{Extension Phase Study Day} = \text{date of event} - \text{start date of Extension phase IP} + 1$<br><br>if date of event < start date of Extension Phase IP, then<br><br>$\text{Extension Phase Study Day} = \text{date of event} - \text{start date of Extension phase IP}$<br><br>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/AIDS-defining 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)]<br><br>as follows:<br><br>If the onset of event falls in Long-term Follow up Phase, then<br><br>• $\text{LTFU Study Day} = \text{date of event} - \text{end date of IP}$ |
| **Study treatment/drugs** |
| • Refers to either investigation product (CAB+RPV oral /CAB+ RPV LA) or ABC/DTG/3TC or DTG plus alternate NRTIs. |

### 13.6.2. Study Population

| Demographics |
|---|
| **Age** |
| • Age, in whole years, will be calculated with respect to the participant's Screening visit.<br>• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:<br>  ○ Any participant with a missing date and month will have this imputed as '30th June'.<br>• Birth date will be presented in listings as 'YYYY'.<br>• Completely missing dates of birth will remain as missing, with no imputation applied. Consequently, the age of the participant will not be calculated and will remain missing. |
| **Body Mass Index (BMI)** |
| • Calculated as **Weight (kg) / Height (m)$^2$,** using Height collected at Day 1. |

## Demographics

### 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 participant will be considered positive for hepatitis B virus (HBV) if they have a positive surface antigen or detectable HBV DNA result during screening. Participants positive for HBV are not allowed to enter the study.

### Lipid-modifying Agents

- The following ATC codes correspond to lipid-modifying agents:
  - ATC Level 2: C10
  - ATC Level 3: C10A, C10B (if Level 2 is not available)
  - ATC Level 4: C10AA, C10AB, C10AC, C10AD, C10AX, C10BA, C10BX (if level 2, 3 are not available)
- Participants 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.
- Participants 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.

### 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:**

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

**for males:**

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

**where**

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

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

**Demographics**

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

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

- A participant will be considered as treated for high blood pressure if during screening it has specified that is suffering from hypertension.
- A participant 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 at Induction Baseline (Week -20). 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 participants who have indicated current or past myocardial infarction conditions on the eCRF. These participants 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), CAB LA+RPV LA, ABC/DTG/3TC (or DTG if alternate NRTI is used) will be calculated from the IP eCRF pages.

| | |
|---|---|
| **Maintenance Phase: Q4W IM arm** | |
| Exposure to CAB + RPV (oral lead-in) = | Oral lead-in CAB/RPV Stop Date – Oral lead-in CAB/RPV Start Date +1 |
| Exposure to CAB LA + RPV LA = | Number of IP injections received during Maintenance Phase (up to but not including Injections administered at Week 100) |
| Overall Exposure to IP = | min [Date of latest Maintenance Phase visit up to and including Week 100, , max (Date of last IP injection +35 [a], Date of last oral CAB/RPV [a] ) ] – Oral lead-in CAB/RPV Start Date +1 |
| **Maintenance + Extension Phase: Q4W IM arm** | |
| Exposure to CAB LA + RPV LA = | Number of IP injections received during Maintenance Phase + Extension Phase |
| Overall Exposure to IP = | min [Date of latest visit, max (Date of last IP injection +35 [a], Date of last oral CAB/RPV [a] )] – Oral lead-in CAB/RPV Start Date +1 |

| | |
|---|---|
| a. Last Q4W IM / last oral dose is only applied to subjects who permanently discontinue from study | |
| **Maintenance Phase: ABC/DTG/3TC arm** | |
| Exposure = Min (Date of latest Maintenance Phase visit up to and including Week 100, Maintenance Phase Treatment Stop Date, Date of Maintenance Phase Discontinuation) – Maintenance Treatment Start Date + 1 | |
| **Extension Phase: ABC/DTG/3TC arm (Extension Switch Population only)** | |
| Exposure to CAB + RPV (oral lead-in) = | Oral lead-in CAB/RPV Stop Date – Oral lead-in CAB/RPV Start Date +1 |
| Exposure to CAB LA + RPV LA = | Number of IP injections received during Extension Phase |
| Overall Exposure to CAB + RPV = | min [Date of latest Extension Phase Visit, max (Date of last IP injection +35 [a], Date of last oral CAB/RPV [a] ) ] – Oral lead-in CAB/RPV Start Date +1 |
| a. Last Q4W IM / last oral dose is only applied to participants who permanently discontinue from study | |

- Duration of dosing in subject years will be calculated as the sum of subject duration of dosing in days (across all subjects)/365.25
- Participants 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.

**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 participant 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 participant 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 Pediatric Adverse Events Version 2.0, November 2014, as specified in the protocol Appendix 12.2.

**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 | |

**Anxiety, Depression and Suicidality/Self-Injury Adverse Events of Special Interest (AESI)**

| **AESI** | **Preferred Term** |
|---|---|
| Anxiety | Anxiety |
| | Anxiety disorder |
| | Anxiety disorder due to a general medical condition |
| | Nervousness |
| | Panic attack |
| Depression | Adjustment disorder with depressed mood |
| | Bipolar disorder |
| | Depressed mood |
| | Depression |
| | Depression suicidal |
| | Major depression |
| | Hypomania |
| | Persistent depressive disorder |
| Suicidality and Self-injury | Intentional self-injury |
| | Self-injurious ideation |
| | Suicidal behaviour |
| | Suicidal ideation |
| | Suicidal attempt |

Note: Additional terms may be added based on blinded review of AE terms collected in the AE dataset prior to database freeze for the respective analysis.

**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) (Levey, 2012)**

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

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

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 $^{Age}$ 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.
- 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 | Hypoglycemia | Hyperglycemia |
| Sodium | Hyponatremia | Hypernatremia |
| Potassium | Hypokalemia | Hyperkalemia |

## Laboratory Parameters

### 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 participant, 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 Maintenance Baseline (Week -20) is calculated as:

$$\% \text{ Change from Maintenance BL} = \frac{\text{Value at Week 48/Week 96} - \text{Maintenance BL value}}{\text{Maintenance BL value}} \times 100\ \%$$

## 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 16) is determined by the last available HIV-1 RNA measurement in that window while the participant is On-treatment in the applicable phase(s), e.g. Maintenance Phase (as assigned based on Table 27).
- When no HIV-1 RNA data is available within a window, a participant cannot be assigned to the category of 'HIV-1 RNA < 50 c/mL'. Depending on the reason for lack of data, the participant 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 participant 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 participant withdraw for reasons other than AE and was not suppressed at the time, they will be a 'HIV-1 RNA≥50 c/mL'.
- 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 (i.e. <2 c/mL) 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 participants who, at the end of the Week 48 analysis window per Table 14 (i.e. study day 350), 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.
- Participants who, at the end of the Week 48 analysis window per Table 14 (i.e. study day 350), 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 (i.e. study day 350) 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].
- See Appendix 15: Variables Defined for Time to Event Analysis for additional details.

**Observed Case Viral Load by Visit Summary Tables**

- 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 participants with on-treatment viral load within the analysis Snapshot visit window (e.g. Week 48 ±6 weeks).
- Numerator: Number of participants 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 Maintenance Baseline (Day 1), 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 Maintenance Baseline (Day 1) to CDC Stage III;
  - CDC Stage II at Maintenance Baseline (Day 1) to CDC Stage III;
  - CDC Stage III at Maintenance Baseline (Day 1) to new CDC Stage III event;
  - CDC Stage I, II, III at Maintenance Baseline (Day 1) 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 Maintenance Baseline (Day 1) and at post-Day 1 during Maintenance Phase will be derived as below:
  - At Baseline (Week -20), the 'Baseline CDC stage' for each participant was assessed by investigator and recorded in the eCRF. However, for the analysis, Maintenance Baseline (Day 1) CDC stage will be derived based on Maintenance Baseline (Day 1) CD4+ values as well as whether any HIV-associated/AIDS-defining conditions present on the start date of maintenance treatment (i.e. started/stopped on Study Day 1 or ongoing through Study Day 1) per the Criteria's thresholds (Appendix 4 in Protocol).
  - To analyse disease progression, the most advanced Maintenance 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 Maintenance Phase CD4+.
- For example, If a participant with CDC 'Stage I' at Maintenance Baseline (Day 1) had the lowest Maintenance Phase CD4+ =120 cell/mm3 without new AIDs-defining conditions, then HIV

disease progression for this participant would be considered as 'CDC stage I at Maintenance Baseline (Day 1) to CDC stage III'.If a participant with CDC 'Stage II' at Maintenance Baseline (Day 1) had the lowest Maintenance Phase CD4+ =220 cell/mm3 AND had at least one new AIDs-defining condition, then HIV disease progression for this participant would be considered as 'CDC stage II at Maintenance Baseline (Day 1) to CDC stage III'.

**Delay in IP Injection**

IM dosing is expected to occur every 4 weeks from Week 4b onwards (for the Q4W arm). The Delay in IP injection (days) will be calculated as:

- 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 participants 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 participant 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.

PK analysis of the plasma CAB concentration-time data on Day 1 and Week 4b for Japan participants will be conducted using non-compartmental methods with WinNonlin (Version 5.2 or higher). Actual sampling and dosing times as recorded in the eCRF will be used for analysis.

**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, excluding samples affected by dosing errors/oral bridging. Sampling windows are determined 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 affected by dosing errors (e.g. wrong dose) or oral bridging will also be excluded.

| Timepoint | Evaluable window | For Programming: |
|---|---|---|
| PRE-DOSE: WK4b/104b 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/104b. |
| 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/104b, 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 participant 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.

## 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.

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.

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.

| Tolerability of Injection (NRS) |
|---|
| **Questionnaire with one single question for Q4W IM arm only** |
| • Maximum level of pain experienced with the most recent injections. Ranking from no pain (0) to extreme pain (10).<br>• Missing scores will be imputed using LOCF (Section 13.7.2.2). |
| **Preference question** |
| Questionnaire with one single dichotomous preference question at Week 48 (Q4W IM arm) |
| • Assess the treatment preference: Months injection vs daily oral current ART at Week 48 for 'Q4W IM' arm<br>• Any missing values will remain missing (i.e. no imputation) |

### 13.6.7. Viral Genotype and Phenotype

| Genotype |
|---|
| **Amino Acid Changes** |
| • A mutation is considered present whenever the encoded amino acid residue differs from the amino acid that would have been encoded by the wild-type (e.g., HXB2, NL43) comparator gene; e.g., Q148K.<br>• 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.<br>• 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 participants (ING112574).

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

- 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]

**Treatment-Emergent Mutations Relative to Induction Baseline (Week -20)**

- Treatment-emergent genotypic mutations are defined as mutations that appear between Induction Baseline (Week -20), i.e. prior to the start of Induction Phase study drug (inclusive), and an on-treatment assessment (e.g., at time of confirmed virologic failure). Note: If Monogram is not able to produce genotype at Week -20, then treatment-emergent will be determined relative to the screening genotype provided by the central laboratory.

**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 below (based on Monogram PhenoSense assay). Clinical cutoffs (where available) or biological cutoffs by PhenoSense will be used to define the phenotypic susceptibility of ART therapy 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 participant'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 may 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:<br>  ○ Randomly assigned to either treatment group, completed the randomized Maintenance Phase including the Nominal Week 100 visit, and did not enter the Extension Phase;<br>  ○ Randomly assigned to either treatment group, completed the randomized Maintenance Phase including the Nominal Week 100 visit, and entered and completed the Extension Phase (defined as remaining on study until commercial supplies of CAB LA + RPV LA become locally available, or development of CAB LA + RPV LA is terminated).<br><br>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 ABC/DTG/3TC 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.<br>• Withdrawn participants were not replaced in the study.<br>• 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.<br>• 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:<br>  ○ 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.<br>  ○ Answers such as “Not applicable” and “Not evaluable” are not considered to be missing data and should be displayed as such. |

| Element | Reporting Detail |
|---|---|
| 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 and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event:<br>○ 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 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.<br>○ 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:<br>○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month<br>○ 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.<br>○ For medications recorded in the eCRF as prior ART, the earlier of this imputed date or the day before Screening date will be used.<br>• The recorded partial date will be displayed in listings. |
| Health outcomes | • For the health outcomes questionnaire data, please refer to Section 13.6.6.<br>• 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, participants 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 on-treatment assessment. |
| Lipid LOCF | **Maintenance Baseline (Day 1) for Lipids LOCF Analyses**:<br>• Last evaluable lipids assessment up to and including the start of Maintenance Phase 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. Participants with unevaluable Maintenance Baseline (Day 1) for Lipids (as defined above) will be excluded from this dataset.<br>**During Maintenance**:<br>• If participants initiate serum lipid-lowering agents during the Maintenance Phase, then the last available fasted On-treatment lipid values prior to the initiation will be used in place of future, observed On-treatment values.<br>• Imputation at visits with observed on-treatment values will continue even if the participant discontinues the lipid-lowering agent. Missing assessments will not be imputed.<br>**Analyses Evaluated with Lipid LOCF dataset:**<br>This dataset will be used to summarize fasting lipids parameters in the following displays:<br>• Summary of Chemistry Values by visit<br>• Summary of Chemistry Change from Maintenance Baseline (Day 1) by visit<br>• Summary of TC/HDL ratio Change from Maintenance Baseline (Day 1)<br>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 Pediatric 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 16 (e.g. window for Week 48 is ± 6 Week: 295 ≤ Study Day ≤ 378) and in Table 14 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 participants 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 participant'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 participants 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. Participants 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 | HIV1-RNA ≥ | Change in |

| | | |
|---|---|---|
| Week 48 AND the latest on-treatment VL prior to/on the date of change is ≥ 50 c/m (NA to this study) | 50 | background therapy |
| 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 | | |
| 5.2.1 if participants still on study i.e. the upper bound of analysis snapshot window is prior to the following date:<br><br>**For ABC/DTG/3TC arm:**<br>Min (ABC/DTG/3TC Stop Date + 1, withdrawal date)<br><br>**For Q4W arm:**<br>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 |

| | | |
|---|---|---|
| 5.2.2 If participants withdraw before/during Week 48 due to | | |
| 5.2.2.1 Safety reasons (e.g. AE/death, liver chemistry stopping criteria, renal toxicity withdrawal criteria, QTc withdrawal criteria et al, as recorded in eCRF Conclusion form) | No virologic data at Week 48 Window | Disc due to AE/death |
| 5.2.2.2 Non-safety related reasons (e.g. Lack of efficacy, protocol deviation, withdrew consent, loss to follow-up, study closed/terminated, investigator discretion et al, as recorded in eCRF Conclusion Form) | | |
| • 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**

1. 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.

2.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 participant 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.

3.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) |
| CVb / CVw | 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 |
| ES | Extension Switch Population |
| FDA | Food and Drug Administration |
| 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 |
|---|---|
| HL | Headline at Week 48 |
| W48 | Week 48 |
| W96 | 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 | SA1 | Summary of Study Populations | CS CORE | HL, W48, W96, EOS |
| 1.2. | All Subjects Screened | Shell TSP1 | Summary of Subjects by Country and Investigator | | W48, W96, EOS |
| 1.3. | All Subjects Screened | ES6 | Summary of Screening Status and Reasons for Screening Failures | CS CORE | W48, W96, EOS |
| 1.4. | All Enrolled | EudraCT age | Summary of Age Categories | CS CORE | W48, W96, EOS |
| 1.5. | ITT-E | ES1 | Summary of Subject Accountability: Study Conclusion Record | ICH E3, GSK CTR, FDAAA, EudraCT | W48, W96, EOS |
| 1.6. | ITT-E | ES1 | Summary of Study Drug Discontinuation | CS CORE | W48, W96, EOS |
| 1.7. | ITT-E | ES1 | Summary of Subject Accountability: Maintenance Phase Conclusion Record | ICH E3, GSK CTR, FDAAA, EudraCT | HL, W48, W96 |

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 1.8. | LTFU | ES1 | Summary of Subject Accountability: Long-term follow up Phase Conclusion Record | ICH E3, GSK CTR, FDAAA, EudraCT | W48, W96, EOS |
| 1.9. | ITT-E | HIV_ES1 | Summary of Subject Accountability: Withdrawals by Visit at Maintenance Phase | | W48, W96 |
| 1.10. | ITT-E | ES1 | Summary of Subject Accountability: Maintenance + Extension Phase Conclusion Record | For Randomized Q4W arm only | W96, EOS |
| 1.11. | ITT-E | HIV_ES1 | Summary of Subject Accountability: Withdrawals by Visit at Maintenance+Extension Phase | For Q4W arm only | W96, EOS |
| 1.12. | ES | ES1 | Summary of Subject Accountability: Extension Phase Conclusion Record – Extension Switch Population | For ABC/DTC/3TC arm only | W96, EOS |
| 1.13. | ES | HIV_ES1 | Summary of Subject Accountability: Withdrawals by Visit (Extension Phase) – Extension Switch Population | For ABC/DTC/3TC arm only | W96, EOS |
| 1.14. | All Participants Enrolled | ES4 | Summary of Subject Disposition at Each Study Epoch | See Mid200056//wk96cdisc/Table 6.1006 | W48, W96, EOS |
| 1.15. | All Participants Enrolled | ES5 | Summary of Reasons for Withdrawal at Each Epoch | See Mid200056//wk96cdisc/Table 6.1007 | W48, W96, EOS |
| 1.16. | ITT-E | DV1a | Summary of Important Protocol Deviations (Maintenance Phase) | CS CORE | W48, W96 |
| 1.17. | ITT-E | DV1a | Summary of Important Protocol Deviations (Maintenance + Extension Phase) | CS CORE<br>For Randomized Q4W arm only | W96, EOS |
| 1.18. | ES | DV1a | Summary of Important Protocol Deviations (Extension Phase) | CS CORE<br>For Randomized ABC/DTG/3TC arm only | W96, EOS |
| 1.19. | ITT-E | SP2 | Summary of Protocol Deviations Leading to Exclusion from the Per-Protocol Population (Maintenance Phase) | CS CORE | W48, W96 |

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 1.20. | ITT-E | IE1 | Summary of Inclusion/Exclusion Criteria Deviations | | W48, W96, EOS |
| 1.21. | All Participants Enrolled | ES1 | Summary of Subject Accountability: Induction Phase Conclusion Record | ICH E3, GSK CTR, FDAAA, EudraCT | W48 |
| **Demography and Baseline** | | | | | |
| 1.22. | ITT-E | Shell TSP2 | Summary of Demographic Characteristics | See also DM1 in IDSL<br>Age categorization will include: <=18, 19-64, >=65 (FDAAA requirement)<br>18-64, 65-84, >=85 (EMA requirement) | HL, W48, W96, EOS |
| 1.23. | ITT-E | DM5 | Summary of Race and Racial Combinations | CS CORE | W48, W96, EOS |
| 1.24. | ITT-E | DM6 | Summary of Race and Racial Combinations Details | CS CORE | W48, W96, EOS |
| 1.25. | ITT-E | Shell TSP3 | Summary of Hepatitis Status at Entry | | W48, W96, EOS |
| 1.26. | ITT-E | CDC1 | Summary of Derived CDC Stages of HIV Infection at Maintenance Baseline (Day 1) | | W48, W96, EOS |
| 1.27. | ITT-E | Shell TSP4 | Summary of Induction Baseline (Week -20) Cardiovascular Risk Assessments | | W48, W96, EOS |
| 1.28. | ITT-E | Shell TSP5 | Distribution of CD4+ Cell Count Results at Maintenance Baseline (Day 1) | Same presentation as shown in the mock shell for induction baseline. | W48, W96, EOS |
| 1.29. | ITT-E | Shell TSP5 | Distribution of Quantitative Plasma HIV-1 RNA and CD4+ Cell Count Results at Screening and Induction Baseline (Week -20) | | W48, W96, EOS |
| **Medical Conditions, Concomitant Medications & Antiretroviral Therapy** | | | | | |
| 1.30. | ITT-E | MH1 | Summary of Current Medical Conditions | CS CORE | W48, W96, EOS |

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 1.31. | ITT-E | MH1 | Summary of Past Medical Conditions | CS CORE | W48, W96, EOS |
| 1.32. | ITT-E | MH4 | Summary of Current Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, Nervous System Conditions, and Hepatobiliary disorders | | W48, W96, EOS |
| 1.33. | ITT-E | MH4 | Summary of Past Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, Nervous System Conditions, and Hepatobiliary disorders | | W48, W96, EOS |
| 1.34. | ITT-E | CM8 | Summary of Concomitant Medication Ingredient Combinations (Maintenance Phase) | | W48, W96 |
| 1.35. | ITT-E | CM8 | Summary of Concomitant Medication Ingredient Combinations (Maintenance + Extension Phase) | For Randomized Q4W arm only | W96, EOS |
| 1.36. | ES | CM8 | Summary of Concomitant Medication Ingredient Combinations (Extension Phase) – Extension Switch Population | For Randomized ABC/DTG/3TC arm only | W96, EOS |
| 1.37. | ITT-E | Shell TSP11 | Summary of Alternate Background NRTI Therapy at End of Induction Phase | | W48, W96, EOS |
| 1.38. | ITT-E | Shell TSP9 | Summary of Lipid Modifying Agent Use at Maintenance Baseline (Day 1) | taken during the 12 weeks before the first Maintenance Phase dose of study drug | W48, W96, EOS |
| 1.39. | ITT-E | Shell TSP10 | Summary of Lipid Modifying Agent Use Started During Maintenance | | W48, W96, EOS |
| 1.40. | ITT-E | SU1 | Summary of Substance Use at Entry | | W48, W96, EOS |
| 1.41. | ITT-E | Shell TSP12 | Summary of HIV Risk Factor | | W48, W96, EOS |
| 1.42. | ITT-E | Shell TSP13 | Summary of Time from First HIV-1 RNA < 50 copies/mL until Initiation of Maintenance Phase Treatment | | W48, W96, EOS |
| 1.43. | ITT-E | Shell CLAD1 | Summary of the Prevalence of HIV-1 Subtype | | |

## 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 | For W96 deliverable, replace 'Week 48' with 'Week 96' | HL, W48, W96 |
| 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 (Per-Protocol Population) | For W96 deliverable, replace 'Week 48' with 'Week 96' | HL, W48, W96 |
| 2.3. | ITT-E | Shell TPEF2 | Summary of Study Outcomes (50 c/mL cut-off) at Week 48 (Maintenance Phase) – Snapshot Analysis | For W96 deliverable, replace 'Week 48' with 'Week 96' | HL, W48, W96 |
| 2.4. | 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 | For W96 deliverable, replace 'Week 48' with 'Week 96' | HL, W48, W96 |
| 2.5. | 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 | For W96 deliverable, replace 'Week 48' with 'Week 96' | W48, W96 |
| 2.6. | ITT-E | Shell TPEF5 | Summary of Study Outcomes (50 c/mL cut-off) at Week 48 by Subgroup (Maintenance Phase) – Snapshot Analysis | For W96 deliverable, replace 'Week 48' with 'Week 96' | W48, W96 |
| **Secondary Efficacy Analyses** | | | | | |
| 2.7. | 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 | For W96 deliverable, replace 'Week 48' with 'Week 96' | HL, W48, W96 |
| 2.8. | 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 (Per-Protocol Population) | For W96 deliverable, replace 'Week 48' with 'Week 96' | HL, W48, W96 |

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 2.9. | 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 | For W96 deliverable, replace 'Week 48' with 'Week 96' | W48, W96 |
| 2.10. | 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 | For W96 deliverable, replace 'Week 48' with 'Week 96' | W48, W96 |
| 2.11. | ITT-E | Shell TSEF2 | Proportion of Subjects with Plasma HIV-1 RNA ≥50 c/mL by Visit (Maintenance Phase) – Snapshot Analysis | | W48, W96 |
| 2.12. | ITT-E | Shell TSEF2.1 | Proportion of Subjects with Plasma HIV-1 RNA ≥50 c/mL by Subgroup and Visit (Maintenance Phase) – Snapshot Analysis | | W48 |
| 2.13. | ITT-E | Shell TSEF7.0 | Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Failure at Week 48 - *Treatment Related Discontinuation = Failure* | For W96 deliverable, replace 'Week 52' with 'Week 100' | W48, W96 |
| 2.14. | ITT-E | Shell TSEF7.1 | Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Failure at Week 48 - *Efficacy Related Discontinuation = Failure* | For W96 deliverable, replace 'Week 52' with 'Week 100' | W48, W96 |
| 2.15. | ITT-E | Shell TSEF2.1 | Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Visit (Maintenance Phase) – Snapshot Analysis | | W48, W96 |
| 2.16. | ITT-E | Shell TSEF2 | Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Subgroup and Visit (Maintenance Phase) – Snapshot Analysis | | W48, W96 |
| 2.17. | ITT-E | Shell TSEF2 | Proportion of Subjects with Plasma HIV-1 RNA <200 c/mL by Visit (Maintenance Phase) – Snapshot Analysis | | W48, W96 |

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 2.18. | 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.<br>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)<br>For W96 deliverable, replace 'Week 48' with 'Week 96' | W48, W96 |
| 2.19. | ITT-E | Shell TSEF8 | Summary of Plasma HIV-1 RNA (log10 c/mL) by Visit | | W48, 96, EOS |
| 2.20. | ITT-E | Shell TSEF3 | Cumulative Proportion of Subjects Meeting Confirmed Virologic Failure Criteria by Visit During the Maintenance Phase (Up to Week 52) | For Week 96 deliverable, show all visit up to Week 100. | HL, W48, W96 |
| 2.21. | ITT-E | Shell TSEF3.1 | Cumulative Proportion of Subjects Meeting Confirmed Virologic Failure Criteria During the Maintenance Phase | | HL, W48, W96 |
| 2.22. | ITT-E | Shell TSEF3.1 | Cumulative Proportion of Subjects Meeting Confirmed Virologic Failure Criteria (Maintenance + Extension Phase) | For Randomized Q4W arm only | W96, EOS |
| 2.23. | ES | Shell TSEF3.1 | Cumulative Proportion of Subjects Meeting Confirmed Virologic Failure Criteria (Extension Phase) – ES population | For Randomized ABC/DTG/3TC arm only | W96, EOS |
| 2.24. | CVF | Shell TSEF4 | Distribution of Quantitative Plasma HIV-1 RNA Results at Suspected and Confirmation of Confirmed Virologic Failure – Maintenance Phase | | W48, W96 |
| 2.25. | ITT-E | Shell TSEF5 | Summary of Change from Maintenance Baseline (Day 1) in CD4+ Cell Count (cells/mm^3) by Visit (Maintenance Phase) | Visits starting from Maintenance Baseline (Day 1), Week 4, … | W48, W96 |

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 2.26. | ITT-E | Shell TSEF5 | Summary of Change from Maintenance Baseline (Day 1) in CD4+ Cell Count (cells/mm^3) by Visit (Maintenance + Extension Phase) | Visits starting from Maintenance Baseline (Day 1), Week 4, … | EOS |
| 2.27. | ES | Shell TSEF5 | Summary of Change from Extension Baseline (Week 100) in CD4+ Cell Count (cells/mm^3) by Visit (Extension Phase) – ES population | | EOS |
| 2.28. | ITT-E | Shell TSEF5 | Summary of Change from Maintenance Baseline (Day 1) in CD4+ Cell Count (cells/mm^3) at Week 48 by Subgroup (Maintenance Phase) | Visits starting from Maintenance Baseline (Day 1), Week 4, …<br>For W96 deliverable, replace 'Week 48' with 'Week 96' | W48, W96 |
| 2.29. | ITT-E | Shell TSEF5 | Summary of CD4+ Cell Count (cells/mm^3) by Visit (Induction + Maintenance Phase) | Visits starting from Induction Baseline (Week -20), Week -16, | W48, W96, EOS |
| 2.30. | ITT-E | Shell TSEF5 | Summary of CD4+ Cell Count (cells/mm^3) by Visit (Maintenance + Extension Phase) | Visits starting from Induction Baseline (Week -20), Week -16, | EOS |
| 2.31. | ES | Shell TSEF5 | Summary of CD4+ Cell Count (cells/mm^3) by Visit (Extension Phase) – ES population | | EOS |
| 2.32. | ITT-E | Shell TSEF5 | Summary of CD8+ Cell Count (cells/mm^3) by Visit (Induction + Maintenance Phase) | Visits starting from Induction Baseline (Week -20), Week -16, | W48, W96, EOS |
| 2.33. | ITT-E | Shell TSEF5 | Summary of CD8+ Cell Count (cells/mm^3) by Visit (Maintenance + Extension Phase) | Visits starting from Induction Baseline (Week -20), Week -16, | EOS |
| 2.34. | ES | Shell TSEF5 | Summary of CD8+ Cell Count (cells/mm^3) by Visit (Extension Phase) – ES population | | EOS |
| 2.35. | ITT-E | Shell TSEF5 | Summary of Change from Maintenance Baseline (Day 1) in CD8+ Cell Count (cells/mm^3) by Visit (Maintenance Phase) | Visits starting from Induction Maintenance Baseline, Week 4, … | W48, W96, |
| 2.36. | ITT-E | Shell TSEF5 | Summary of Change from Maintenance Baseline (Day 1) in CD8+ Cell Count (cells/mm^3) by Visit (Maintenance + Extension Phase) | Visits starting from Maintenance Baseline (Day 1), Week 4, … | EOS |

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 2.37. | ITT-E | Shell TSEF5 | Summary of Change from Maintenance Baseline (Day 1) in CD8+ Cell Count (cells/mm^3) by Visit (Extension Phase) – ES Population | | EOS |
| 2.38. | ITT-E | Shell TSEF5 | Summary of CD4+/CD8+ Ratio Cell Count (cells/mm^3) by Visit Induction + Maintenance Phase) | While both CD4+ and CD8+ are available on the same date | W48, W96 |
| 2.39. | ITT-E | Shell TSEF5 | Summary of CD4+/CD8+ Ratio Cell Count (cells/mm^3) by Visit Induction + Maintenance + Extension Phase) | For Randomized Q4W arm only | EOS |
| 2.40. | ES | Shell TSEF5 | Summary of CD4+/CD8+ Ratio Cell Count (cells/mm^3) by Visit (Extension Phase) – ES Population | | EOS |
| 2.41. | ITT-E | HIV1/Shell TSEF 6.0 | Summary of Maintenance Phase HIV-1 Associated Conditions Including Recurrences | | W48, W96 |
| 2.42. | ITT-E | HIV1/Shell TSEF 6.0 | Summary of HIV-1 Associated Conditions Including Recurrences (Maintenance + Extension Phase) | For Randomized Q4W arm only | EOS |
| 2.43. | ES | HIV1/Shell TSEF 6.0 | Summary of HIV-1 Associated Conditions Including Recurrences (Extension Phase) – ES Population | | EOS |
| 2.44. | ITT-E | HIV1/Shell TSEF 6.0 | Summary of Maintenance Phase HIV-1 Associated Conditions Excluding Recurrences | | W48, W96 |
| 2.45. | ITT-E | HIV1/Shell TSEF 6.0 | Summary of HIV-1 Associated Conditions Excluding Recurrences (Maintenance + Extension Phase) | For Randomized Q4W arm only | EOS |
| 2.46. | ES | HIV1/Shell TSEF 6.0 | Summary of HIV-1 Associated Conditions Excluding Recurrences (Extension Phase) – ES Population | | EOS |
| 2.47. | ITT-E | HIV2/Shell TSEF6.1 | Summary of HIV-1 Disease Progression and/or Deaths (Maintenance Phase) | | W48, W96 |
| 2.48. | ITT-E | HIV2/Shell TSEF6.1 | Summary of HIV-1 Disease Progressions and/or Deaths (Maintenance + Extension Phase) | For Randomized Q4W arm only | EOS |
| 2.49. | ES | HIV2/Shell TSEF6.1 | Summary of HIV-1 Disease Progressions – ES Population | | EOS |
| 2.50. | ITT-E | TSEF12 | Proportion of Subjects with Plasma HIV-1 RNA <2 copies/mL by Visit - Observed Case Analysis (Maintenance Phase) | | W48, W96 |

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 2.51. | ITT-E | Shell TPEF2 | Summary of Study Outcomes (200 c/mL) at Week 48 (Maintenance Phase) – Snapshot Analysis | For W96 analysis, replace 'Week 48' with 'Week 96' | W48, W96 |
| 2.52. | ITT-E | Shell TSEF11 | Summary of Subjects per Viral Load Category by Visit (Maintenance Phase) | | W48, W96 |
| 2.53. | All Participants Enrolled | Shell TSEF12 | Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Visit (Observed data) – Induction Phase | Induction Baseline (Week -20), Week -16, Week -8, Week -4 and Day 1. Single arm for Induction ABC/DTG/3TC | W48 |

## 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 (Maintenance Phase) – Snapshot Analysis | | W48, W96 |
| 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 | For W96 deliverable, replace 'Week 48' with 'Week 96' | W48, W96 |
| **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 | | W48, W96 |
| 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 | For W96 analysis, replace 'Week 48' with 'Week 96' | W48, W96 |

| 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 | | W48, W96 |
| 2.6. | ITT-E | Mid200056//wk96cdisc/Figure 7.1007 | Individual Plasma HIV-1 RNA (log10 copies/mL) Profiles by Visit– for CVF subjects (Randomized Q4W) | The first vertical line indicates start of Induction phase investigational product (ABC/DTG/3TC or DTG). The second vertical line indicates start of Maintenance phase investigational product (oral CAB + oral RPV). The third vertical reference line indicates last on-treatment study day, i.e. min(max(day of last IP injection dose+35 days, day of last oral CAB+RPV+1, day of LTFU HAART start date). This line is only for participants who withdraw from the Maintenance/Extension phase. | HL, W48, W96, 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 (ABC/DTG/3TC) | The first vertical line indicates start of Induction phase investigational product (ABC/DTG/3TC or DTG). The second vertical line indicates start of Maintenance phase investigational product (continuation of ABC/DTG/3TC or DTG). The third vertical reference line indicates last Maintenance phase on-treatment study day, i.e. day of last ABC/DTG/3TC (or DTG) dose + 1. This line is only for participants who withdraw or complete the Maintenance phase. The fourth vertical reference line indicates last Extension Phase on-treatment study day, i.e. min(max(day of last IP injection dose+35 days, day of last oral CAB+RPV+1, day of LTFU HAART start date). This line is only for participants who withdraw from the Extension phase. | HL, W48, W96, EOS |
| 2.8. | ITT - E | Mid200056//wk96cdisc/Figure 7.1007 | Individual Plasma HIV-1 RNA for subjects who are in the category of 'HIV-1 RNA ≥50 c/mL' at Week 48 per Snapshot algorithm (randomized Q4W arm) | The first vertical line indicates start of Induction phase investigational product (ABC/DTG/3TC or DTG). The second vertical line indicates start of Maintenance phase investigational product (oral CAB + oral RPV). The third vertical | HL, W48, W96, EOS |

| Efficacy: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| | | | | reference line indicates last on-treatment study day, i.e.min(max(day of last IP injection dose+35 days, day of last oral CAB+RPV+1, day of LTFU HAART start date). This line is only for participants who withdraw from the Maintenance/Extension phase. | |

| Efficacy: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 2.9. | ITT - E | Mid200056//wk 96cdisc/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 ABC/DTG/3TC arm) | The first vertical line indicates start of Induction phase investigational product (ABC/DTG/3TC or DTG). The second vertical line indicates start of Maintenance phase investigational product (continuation of ABC/DTG/3TC or DTG). The third vertical reference line indicates last Maintenance phase on-treatment study day, i.e. day of last ABC/DTG/3TC (or DTG) dose + 1. This line is only for participants who withdraw or complete the Maintenance phase.The fourth vertical reference line indicates last Extension Phase on-treatment study day, i.e. min(max(day of last IP injection dose+35 days, day of last oral CAB+RPV+1, day of LTFU HAART start date). This line is only for participants who withdraw from the Extension phase. | HL, W48, W96, EOS |
| 2.10. | ITT - E | Shell FPEF1 | Proportion (95% CI) of Subjects with HIV-1 RNA >=200 c/mL by Visit – Snapshot Analysis | | W48, W96 |

## 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 | W48, W96, 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) | W96, EOS |
| 3.3. | ES | Shell TS1.1 | Summary of Extent of Exposure to Investigational Product – Extension Phase | CS Core (only for ABC/DTG/3TC) | W96, EOS |
| 3.4. | Safety | Shell TS1.2 | Summary of Needle Length and Gauge for CAB Injection - Maintenance Phase | (only for Q4W arm) | W48, W96 |
| 3.5. | Safety | Shell TS1.2 | Summary of Needle Length and Gauge for RPV Injection - Maintenance Phase | (only for Q4W arm) | W48, W96 |
| 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 | W48, W96 |
| **Adverse Events** | | | | | |
| 3.7. | Safety | AE1 | Summary of All Adverse Events by System Organ Class – Maintenance Phase | CS Core | W48, W96 |
| 3.8. | Safety | AE5B | Summary of All Adverse Events by System Organ Class and Maximum Toxicity – Maintenance Phase | CS Core | HL, W48, W96 |
| 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) | W96, EOS |
| 3.10. | ES | AE5B | Summary of All Adverse Events by System Organ Class and Maximum Toxicity – Extension Phase (Extension Switch) | CS Core (only for ABC/DTG/3TC arm) | W96, EOS |
| 3.11. | Safety | AE5B | Summary of All On-treatment Adverse Events by System Organ Class and Maximum Toxicity – Maintenance Phase | CS Core | W48, W96 |

| **Safety Tables (**Displays will be for both treatment arms, unless specified | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.12. | LTFU | AE5B | Summary of All Adverse Events by System Organ Class and Maximum Toxicity – Long-term Follow-up Phase | CS Core | 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, W48 |
| 3.14. | Safety | AE3 | Summary of Common Adverse Events (>=5%) by Overall Frequency – Maintenance Phase | CS Core | W48, W96 |
| 3.15. | Safety | AE3 | Summary of Common Grade 2-5 Adverse Events (>=1%) by Overall Frequency – Maintenance Phase | | W48, W96 |
| 3.16. | Safety | AE1 | Summary of All Drug-Related Adverse Events by System Organ Class– Maintenance Phase | | W48, W96 |
| 3.17. | Safety | AE5B | Summary of All Drug-Related Adverse Events by System Organ Class and Maximum Toxicity – Maintenance Phase | CS Core | HL, W48, W96 |
| 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) | W96, EOS |
| 3.19. | ES | AE5B | Summary of All Drug-Related Adverse Events by System Organ Class and Maximum Toxicity – Extension Phase | CS Core (for ABC/DTG/3TC only) | W96, EOS |
| 3.20. | Safety | AE3 | Summary of All Drug-Related Grade 2-5 Adverse Events by Overall Frequency – Maintenance Phase | | W48, W96 |
| **Serious and Other Significant Adverse Events** | | | | | |
| 3.21. | Safety | AE1 | Summary of Serious Adverse Events by System Organ Class – Maintenance Phase | CS Core | HL, W48, W96 |
| 3.22. | Safety | AE1 | Summary of Serious Adverse Events by System Organ Class – Maintenance +Extension Phase | CS Core (for Q4W arm only) | W96, EOS |
| 3.23. | ES | AE1 | Summary of Serious Adverse Events by System Organ Class – Extension Phase | CS Core (for ABC/DTG/3TC arm only) | W96, EOS |
| 3.24. | LTFU | AE1 | Summary of Serious Adverse Events by System Organ Class – Long term follow up | CS Core | W48, W96, EOS |

| **Safety Tables (**Displays will be for both treatment arms, unless specified | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.25. | Safety | AE1 | Summary of Serious Adverse Events by System Organ Class — Oral Lead-in Period at Maintenance Phase | CS Core for Q4W only | HL, W48 |
| 3.26. | Safety | AE1 | Summary of Drug-Related Serious Adverse Events by System Organ Class – Maintenance Phase | CS Core | W48, W96 |
| 3.27. | Safety | AE1 | Summary of Drug-Related Serious Adverse Events by System Organ Class – Maintenance + Extension Phase | CS Core (for Q4W arm only) | W96, EOS |
| 3.28. | ES | AE1 | Summary of Drug-Related Serious Adverse Events by System Organ Class – Extension Phase | CS Core (for Current arm only) | W96, EOS |
| 3.29. | Safety | AE3 | Summary of Non-Fatal Serious Adverse Events by Overall Frequency – Maintenance Phase | | W48, W96 |
| 3.30. | Safety | AE3 | Summary of Drug-Related Non-Fatal Serious Adverse Events by Overall Frequency – Maintenance Phase | | W48, W96 |
| 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, W48, W96 |
| 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) | W96, EOS |
| 3.33. | ES | AE1 | Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by SOC – Extension Phase | CS Core (for ABC/DTG/3TC arm only) | W96, EOS |
| 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) | W48, W96 |
| 3.35. | Safety | AE1 | Summary of Common (>=5%) Non-Serious Adverse Events – Maintenance Phase | CS Core | W48, W96 |

| **Safety Tables (**Displays will be for both treatment arms, unless specified | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 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 | W48, W96 |
| 3.37. | Safety | EudraCT SAE AE16 | Summary of Subjects and Number of Occurrences of SAEs, Fatal SAEs, and Drug-related SAEs – Maintenance Phase | CS Core for FDAAA and EMA disclosure requirements. EudraCT | W48, W96 |
| 3.38. | Safety | Shell TS2.1 | Summary of Cumulative Adverse Events by Visit– Maintenance Phase | Please note this table only display AEs occurring >=5% subjects during Maintenance Phase | W48, W96 |
| 3.39. | All Participants Enrolled | AE1 | Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by System Organ Class– Induction Phase | CS Core | W48 |
| **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, W48, W96 |
| 3.41. | Safety | Shell TS2.2 | Summary of Injection Site Reaction Adverse Events (Event-Level Summary) –Maintenance + Extension Phase | (for Q4W arm only) | W96, EOS |
| 3.42. | ES | Shell TS2.2 | Summary of Injection Site Reaction Adverse Events (Event-Level Summary) –Extension Phase | (for ABC/DTG/3TC arm only) | W96, EOS |
| 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) | W48, W96 |
| 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) | W96, EOS |

| **Safety Tables (**Displays will be for both treatment arms, unless specified | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.45. | ES | 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 ABC/DTG/3TC arm only) | W96, 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) | W48, W96 |
| 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) | W48, W96 |
| 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) | W48, W96 |
| 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) | W48, W96 |
| 3.50. | Safety | Shell TS2.5 | Summary of Maximum Drug-Related Injection Site Reaction Adverse Event Grade by Needle Length (Maintenance Phase) – CAB (common ISRs) | Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects (for Q4W arm only) | W48, W96 |
| 3.51. | Safety | Shell TS2.2 | Summary of Drug-Related Injection Site Reaction Adverse Events (Event-Level Summary) - RPV (Maintenance Phase) | | W48, W96 |
| 3.52. | Safety | Shell TS2.3 | Summary of Drug-Related Subject-Level Characteristics of Injection Site Reaction Adverse Events (Maintenance Phase) - | Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects (for Q4W | W48, W96 |

| **Safety Tables (**Displays will be for both treatment arms, unless specified | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| | | | Overall and Common (RPV) | arm only) | |
| 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 | | W48, W96 |
| 3.54. | Safety | Shell TS2.5 | Summary of Maximum Drug-Related Injection Site Reaction Adverse Event Grade by Needle Length (Maintenance Phase) – RPV (common ISRs) | Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects (for Q4W arm only) | W48, W96 |
| **Laboratory: Chemistry, Hematology and Renal Markers** | | | | | |
| 3.55. | Safety | LB1 | Summary of Chemistry Changes from Maintenance Baseline (Day 1) by Visit (Maintenance Phase) | CS Core (include lipids and glucose in Conventional Units, renal markers of Retinol Binding Protein, Cystatin C, and CKD-EP1 GFR using Creatinine, and CKD-EP1 using Cystatin C et al | W48, W96 |
| 3.56. | Safety | LB1 | Summary of Chemistry Changes from Maintenance Baseline (Day 1) by Visit (Maintenance + Extension Phase) | CS Core (include lipids and glucose in Conventional Units, renal markers of Retinol Binding Protein, Cystatin C, and CKD-EP1 GFR using Creatinine, and CKD-EP1 using Cystatin C et al) | W96, EOS |
| 3.57. | ES | LB1 | Summary of Chemistry Changes from Extension Baseline (Week 100) by Visit (Extension Phase) – ES population | CS Core (include lipids and glucose in Conventional Units, renal markers of Retinol Binding Protein, Cystatin C, and CKD-EP1 GFR using Creatinine, and CKD-EP1 using Cystatin C et al) | W96, EOS |

| **Safety Tables (**Displays will be for both treatment arms, unless specified | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.58. | Safety | LB1 | Summary of Chemistry Values by Visit (Maintenance Phase) | (include lipids and glucose in Conventional Units, renal markers of Retinol Binding Protein, Beta-2 Microglobulin, Cystatin C, et al) | W48, W96 |
| 3.59. | Safety | LB1 | Summary of Chemistry Values by Visit (Maintenance + Extension Phase) | (include lipids and glucose in Conventional Units, renal markers of Retinol Binding Protein, Beta-2 Microglobulin, Cystatin C, et al) | W48, W96 |
| 3.60. | ES | LB1 | Summary of Chemistry Values by Visit (Extension Phase) – ES Population | (include lipids and glucose in Conventional Units, renal markers of Retinol Binding Protein, Beta-2 Microglobulin, Cystatin C, et al) | W96 |
| 3.61. | Safety | LB1 | Summary of Hematology Changes from Maintenance Baseline (Day 1) by Visit (Maintenance Phase) | CS Core | W48, 96, EOS |
| 3.62. | Safety | LB1 | Summary of Hematology Changes from Maintenance Baseline (Day 1) by Visit (Maintenance + Extension Phase) | CS Core | W96, EOS |
| 3.63. | ES | LB1 | Summary of Hematology Changes from Maintenance Baseline (Day 1) by Visit (Extension Phase) – ES Population | CS Core | W96, EOS |
| 3.64. | Safety | LB1 | Summary of Hematology Values by Visit (Maintenance Phase) | CS Core | W48, 96, EOS |
| 3.65. | Safety | LB1 | Summary of Hematology Values by Visit (Maintenance + Extension Phase) | CS Core | W96, EOS |
| 3.66. | ES | LB1 | Summary of Hematology Values by Visit (Extension Phase) – ES Population | CS Core | W96, EOS |
| 3.67. | Safety | Shell TS9.1 | Summary of Maximum Maintenance Phase Emergent Chemistry Toxicities | CS Core | W48, W96 |
| 3.68. | Safety | Shell TS9.2 | Summary of Maximum Maintenance and Extension Phase Emergent Chemistry Toxicities (Randomized Q4W) | CS Core (for Q4W arm only) | W96, EOS |
| 3.69. | ES | Shell TS9.3 | Summary of Maximum Extension Phase Emergent Chemistry | CS Core (for ABC/DTG/3TC arm | W96, EOS |

| **Safety Tables (**Displays will be for both treatment arms, unless specified | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| | | | Toxicities –ES Population | only) | |
| 3.70. | Safety (Q4W IM only) | Shell TS9.2 | Summary of Maximum Maintenance Phase Emergent Chemistry Toxicities – Maintenance Phase Oral Lead-in Period | CS Core (for Q4W arm only) | W48 |
| 3.71. | Safety | Shell TS9.1 | Summary of Maximum Maintenance Phase Emergent Hematology Toxicities | CS Core | W48, W96 |
| 3.72. | Safety | Shell TS9.2 | Summary of Maximum Maximum Maintenance and Extension Phase Emergent Hematology Toxicities (Randomized Q4W) | CS Core (for Q4W arm only) | W96, EOS |
| 3.73. | ES | Shell TS9.3 | Summary of Maximum Extension Phase Emergent Hematology Toxicities - ES Population | CS Core (for ABC/DTG/3TC arm only | W96, EOS |
| 3.74. | Safety (Q4W IM only) | Shell TS9.2 | Summary of Maximum Maintenance Phase Emergent Hematology Toxicities – Maintenance Phase Oral Lead-in Period | CS Core (for Q4W arm only) | W48 |
| 3.75. | Safety | Shell TS16 | Summary of Fasting Lipids Percentage Changes from Maintenance Baseline (Day 1) by Visit (Lipid LOCF)– Maintenance Phase | | W48, W96 |
| **Laboratory: Urinalysis** | | | | | |
| 3.76. | Safety | UR3 or SHELL TS3 | Summary of Urinalysis Dipstick Results by Visit (Maintenance Phase) | | W48, W96, EOS |
| 3.77. | Safety | UR3 or SHELL TS3 | Summary of Urinalysis Dipstick Results by Visit (Maintenance + Extension Phase) | CS Core (for Q4W arm only) | W96, EOS |
| 3.78. | ES | UR3 or SHELL TS3 | Summary of Urinalysis Dipstick Results by Visit (Extension Phase) – ES Population | CS Core (for ABC/DTG/3TC arm only | W96, EOS |
| 3.79. | Safety | LB1 | Summary of Urine Concentrations Changes from Maintenance Baseline (Day 1) by Visit (Maintenance Phase) | CS Core | W48, W96, EOS |
| 3.80. | Safety | LB1 | Summary of Urine Concentrations Changes from Maintenance Baseline (Day 1) by Visit (Maintenance + Extension Phase) | CS Core | W96, EOS |
| 3.81. | Safety | LB1 | Summary of Urine Concentrations Changes from Maintenance Baseline (Day 1) by Visit (Extension Phase) – ES Population | CS Core | W96, EOS |

| **Safety Tables (**Displays will be for both treatment arms, unless specified | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.82. | Safety | Shell TS4 | Summary of Changes in Proteinuria Maintenance Baseline (Day 1) Laboratory Result to Maximum Maintenance Phase Laboratory Result (Maintenance Phase) | | W48, W96 |
| **Laboratory: NCEP Lipid and Markers** | | | | | |
| 3.83. | Safety | Shell TS5 | Summary of Changes in Maintenance Baseline (Day 1) NCEP Fasting Lipid Category to Maximum Maintenance Phase Category - Triglycerides | | W48, W96 |
| 3.84. | Safety | Shell TS5 | Summary of Changes in Maintenance Baseline (Day 1) NCEP Fasting Lipid Category to Maximum Maintenance Phase Category – Total Cholesterol | | W48, W96 |
| 3.85. | Safety | Shell TS5 | Summary of Changes in Maintenance Baseline (Day 1) NCEP Fasting Lipid Category to Maximum Maintenance Phase Category – HDL Cholesterol | | W48, W96 |
| 3.86. | Safety | Shell TS5 | Summary of Changes in Maintenance Baseline (Day 1) NCEP Fasting Lipid Category to Maximum Maintenance Phase Category – LDL Cholesterol | | W48, W96 |
| 3.87. | Safety | Shell TS6 | Summary of Fasting TC/HDL ratio Changes from Maintenance Baseline (Day 1) (Maintenance Phase) – Lipids LOCF | | W48, W96 |
| 3.88. | Safety | Shell TS7 | Summary of Bone Markers Changes from Maintenance Baseline (Day 1) (Maintenance Phase) | | W48, W96 |
| 3.89. | Safety | Shell TS7 | Summary of Bone Markers Values (Maintenance Phase) | | W48, W96 |
| 3.90. | Safety | Shell TS8 | Statistical Analysis of Log-Transformed Ratio to Maintenance Baseline (Day 1) in Bone Markers at Week 48 – Observed Case | For W96, replace Week 48 with W96. | W48, W96 |
| **Laboratory: Hepatobiliary (Liver)** | | | | | |
| 3.91. | Safety | Liver1 /Shell TS11 | Summary of Liver Monitoring/Stopping Event Reporting (Maintenance Phase) | | W48, W96 |
| 3.92. | Safety | liver10/Shell TS12 | Summary of Subjects Meeting Hepatobiliary Abnormality Criteria (Maintenance Phase) | | W48, W96 |

| **Safety Tables (**Displays will be for both treatment arms, unless specified | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.93. | Safety | liver10/Shell TS12 | Summary of Subjects Meeting Hepatobiliary Abnormality Criteria (Maintenance + Extension Phase) | (for Q4W arm only) | W96, EOS |
| 3.94. | ES | liver10/Shell TS12 | Summary of Subjects Meeting Hepatobiliary Abnormality Criteria (Extension Phase) | CS Core (for ABC/DTG/3TC arm only | W96, EOS |
| 3.95. | Safety (Q4W arm only) | liver10/Shell TS12 | Summary of Subjects Meeting Hepatobiliary Abnormality Criteria–Maintenance Phase Oral Lead-in Period | (for Q4W arm only) | WK48 |
| **ECG** | | | | | |
| 3.96. | Safety | EG1 | Summary of ECG Findings (Maintenance Phase) | | WK48 |
| 3.97. | ES | EG1 | Summary of ECG Findings (Extension Phase) | CS Core (for ABC/DTG/3TC arm only | WK96, EOS |
| 3.98. | Safety | EG2 | Summary of Change from Maintenance Baseline (Day 1) in ECG values by Visit (Maintenance Phase) | | WK48, 96, EOS |
| 3.99. | Safety | EG10 | Summary of QTc Values by Category (Maintenance Phase) | Mid200056/wk48idsl/Table 8.1043 | W48, W96 |
| 3.100. | ES | EG10 | Summary of QTc Values by Category (Extension Phase) | Mid200056/wk48idsl/Table 8.1043 (Switch Arm only) | W96 |
| 3.101. | Safety | EG10 | Summary of Change from Maintenance Baseline (Day 1) QTc Values by Category (Maintenance Phase) | Mid200056/wk48idsl/Table 8.1044 | W48, W96 |
| 3.102. | ES | EG10 | Summary of Change from Maintenance Baseline (Day 1) QTc Values by Category (Extension Phase) | Mid200056/wk48idsl/Table 8.1044(for Switch arm only) | W96, EOS |
| **eC-SSR and Others** | | | | | |
| 3.103. | Safety | VS1 | Summary of Change from Maintenance Baseline (Day 1) in Vital Signs by Visit (Maintenance Phase) | CS Core | W48, W96 |
| 3.104. | Safety | Shell TS14 | Summary of Subjects with eC-SSRS Suicidal Ideation or Behaviour During the Maintenance Phase | | W48, W96 |

| **Safety Tables (**Displays will be for both treatment arms, unless specified | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.105. | Safety | Shell TS14.1 | Summary of Depression and Suicidal and Self-Injury Adverse Events by System Organ Class, Maximum DAIDS Toxicity Grade, and History of Depression, Anxiety and Suicidal and Self-Injury at Screening (Maintenance Phase) | See preferred terms specified in Section 13.6.3 | W48, W96 |
| 3.106. | Safety | VS1 | Summary of Change from Induction Baseline (Week -20) in Weight and BMI by Visit (Maintenance Phase) | CS Core | W48, W96 |
| 3.107. | Safety | AE5B | Summary of All Adverse Events Excluding Injection Site Reactions by System Organ Class and Maximum Toxicity – Maintenance Phase | CS Core | HL, W48, W96 |
| 3.108. | Safety | AE5B | Summary of All Drug-Related Adverse Events Excluding Injection Site Reactions by System Organ Class and Maximum Toxicity – Maintenance Phase | CS Core | HL, W48, W96 |

## 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 ABC/DTG/3TC (Maintenance Phase) – Excluding ISRs | CS CORE | HL, W48, W96 |
| 3.2. | Safety | LIVER9 | Scatter Plot of Maximum vs. Baseline for ALT (Maintenance Phase) | CS CORE | HL, W48, W96 |
| 3.3. | Safety | LIVER9 | Scatter Plot of Maximum ALT vs. Maximum Total Bilirubin (Maintenance Phase) | CS CORE | HL, W48, W96 |
| 3.4. | Safety | Shell FS2/ | Matrix Plot of Maximum Liver Chemistries at Maintenance Phase | CS CORE | HL, W48, W96 |
| 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 and/or RPV | Repeat parameters for CAB, RPV (for Q4W arm only) | W48, W96 |
| 3.6. | Safety | Shell FS3/ | Plot of Onset, Duration, and Severity of Overall and Common Maintenance Phase Drug-Related Injection Site Reaction AEs by Maximum Grade – CAB | Repeat parameters for CAB, RPV (for Q4W arm only) | W48, W96 |
| 3.7. | Safety | Shell FS3/ | Plot of Onset, Duration, and Severity of Overall and Common Maintenance Phase Drug-Related Injection Site Reaction AEs by Maximum Grade – RPV | Repeat parameters for CAB, RPV (for Q4W arm only) | W48, W96 |
| 3.8. | Safety | Shell FS4/ | Plot of Incidence of Maintenance Phase Injection Site Reaction Adverse Events by Visit (Overall and Common) – CAB and/or RPV | Repeat parameters for CAB, RPV (for Q4W arm only) | W48, W96 |
| 3.9. | Safety | Shell FS4/ | Plot of Incidence of Maintenance Phase Drug-Related Injection Site Reaction Adverse Events by Visit (Overall and Common) – CAB | Repeat parameters for CAB, RPV (for Q4W arm only) | W48, W96 |
| 3.10. | Safety | Shell FS4/ | Plot of Incidence of Maintenance Phase Drug-Related Injection Site Reaction Adverse Events by Visit (Overall and Common) – RPV | Repeat parameters for CAB, RPV (for Q4W arm only) | W48, W96 |

| Safety: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.11. | Safety | Shell FS4/ | Plot of Incidence of Grade 3-5 Maintenance Phase Injection Site Reaction Adverse Events by Visit (Overall and Common) — CAB and/or RPV | Repeat parameters for CAB, RPV (for Q4W arm only) | W48, W96 |
| 3.12. | Safety | Shell FS1 | Bar Chart of Lipid NCEP Categories at Week 48 vs. Maintenance Baseline (Day 1) – Triglycerides, Total Cholesterol, LDL Cholesterol | For W96, replace W48 with W96<br>Example: arenv/arprod/gsk3365791/mid_dori_ph3/week48/outputs/Figure 3.062 | W48, W96 |
| 3.13. | Safety | Shell FS1 | Bar Chart of Lipid NCEP Categories at Week 48 vs. Maintenance Baseline (Day 1) - HDL Cholesterol | For W96, replace W48 with W96<br>Example: arenv/arprod/gsk3365791/mid_dori_ph3/week48/outputs/Figure 3.062 | |

## 13.13.9. Pharmacokinetic Tables

| Pharmacokinetic: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes**<br>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<br>Visits up to W52 for the W48 deliverable. | W48, W96 |
| 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<br>Visits up to W52 for the W48 deliverable. | W48, W96 |

| 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]** |
| 4.3. | PK | PKCT1 | Summary of Evaluable Plasma CAB PK Concentration (ug/mL)-Time Data by Treatment and Visit – Included Log-transformed Statistics | Table 10.1012<br>Visits up to W52 for the W48 deliverable. | W48, W96 |
| 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<br>Visits up to W52 for the W48 deliverable. | W48, W96 |
| 4.5. | PK | Shell TPK01 | Summary of Results of Steady State Assessment | Table 10.1005<br>Visits up to W52 for the W48 deliverable. | W48 |
| 4.6. | PK | Shell TPK01 | Summary of Results of Steady State Assessment- Evaluable concentration | Table 10.1009<br>Visits up to W52 for the W48 deliverable. | W48 |
| 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) | W96 |
| 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) | W96 |

## 13.13.10. 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<br>Visits up to W52 for the W48 deliverable. | W48, W96 |
| 4.2. | PK | PKCF1 | Individual Plasma RPV Concentration-Time Plots (Linear and Semi-Log) | Figure 10.1002<br>Visits up to W52 for the W48 deliverable. | W48, W96 |
| 4.3. | PK | PKCF2 | Mean (SD) Plasma CAB Concentration-Time Plots (Linear and Semi-Log) | Figure 10.1003<br>Visits up to W52 for the W48 deliverable. | W48, W96 |
| 4.4. | PK | PKCF3 | Median ($5^{th}$ and $95^{th}$ percentile) Plasma CAB Concentration-Time Plots (Linear and Semi-Log) | Figure 10.1004<br>Visits up to W52 for the W48 deliverable. | W48, W96 |
| 4.5. | PK | PKCF2 | Mean (SD) Plasma RPV Concentration-Time Plots (Linear and Semi-Log) | Figure 10.1005<br>Visits up to W52 for the W48 deliverable. | W48, W96 |
| 4.6. | PK | PKCF3 | Median ($5^{th}$ and $95^{th}$ percentile) Plasma RPV Concentration-Time Plots (Linear and Semi-Log) | Figure 10.1006<br>Visits up to W52 for the W48 deliverable. | W48, W96 |
| 4.7. | PK | PKCF2 | Mean (SD) Evaluable Plasma CAB Concentration-Time Plots (Linear and Semi-Log) | Figure 10.1007<br>Visits up to W52 for the W48 deliverable. | W48, W96 |
| 4.8. | PK | PKCF3 | Median ($5^{th}$ and $95^{th}$ percentile) Evaluable Plasma CAB Concentration-Time Plots (Linear and Semi-Log) | Figure 10.1008<br>Visits up to W52 for the W48 deliverable. | W48, W96 |

| Pharmacokinetic: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** The mock-up below from study 200056 (week48idsl) | **Deliverable [Priority]** |
| 4.9. | PK | PKCF2 | Mean (SD) Evaluable Plasma RPV Concentration-Time Plots (Linear and Semi-Log) | Figure 10.1009 Visits up to W52 for the W48 deliverable. | W48, W96 |
| 4.10. | PK | PKCF3 | Median ($5^{th}$ and $95^{th}$ percentile) Evaluable Plasma RPV Concentration-Time Plots (Linear and Semi-Log) | Figure 10.1010 Visits up to W52 for the W48 deliverable | W48, W96 |
| 4.11. | PK | PKCF2 | Mean (SD) Evaluable Plasma CAB Concentration-Time Plots (Semi-Log) | Figure 10.1011 Visits up to W52 for the W48 deliverable | W48, W96 |
| 4.12. | PK | PKCF2 | Mean (SD) Evaluable Plasma RPV Concentration-Time Plots (Semi-Log) | Figure 10.1012 Visits up to W52 for the W48 deliverable | W48, W96 |

## 13.13.11. 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. | PK | Shell TPK03/Table 11.1007 (see applicable subgroups in Section 5.4.2) | Logistic Regression Analysis of Snapshot 'HIV-1 RNA≥50 c/mL' at Week 48 by Trough PK Concentration and subgroup –univariable analysis | Last Trough Concentration and Nominal Week-8 trough PK concentration will be treated both as continuous variable and as subgroup.<br><br>For W96 delivery, replace Week 48 with Week 96 | W48, W96 |
| 5.2. | PK | Shell TPK03/Table 11.1008 | Multivariable Logistic Regression Analysis of Predictors of Snapshot 'HIV-1 RNA≥50 c/mL' at Week 48 | For W96 delivery, replace Week 48 with Week 96 | W48, W96 |
| 5.3. | PK | Shell TPK02 | Summary of Last trough CAB PK concentration by Snapshot Virologic Response at Week 48– Included Log-transformed Statistics | The Virologic Response include: WK48 Snapshot HIV-1 RNA>=50 (Yes/No)<br><br>For W96 delivery, replace Week 48 with Week 96 | W48, W96 |

| Pharmacokinetic / Pharmacodynamic: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** The similar outputs below from study 200056 (week48idsl) | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 5.4. | PK | Shell TPK02 | Summary of Last trough RPV PK concentration by Snapshot Virologic Response at Week 48 – Included Log-transformed Statistics | Same as above | W48, W96 |
| 5.5. | PK | Shell TPK02 | Summary of Week 8 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)<br>For W96 delivery, replace Week 48 with Week 96 | W48, W96 |
| 5.6. | PK | Shell TPK02 | Summary of Week 8 trough RPV PK concentration by Virologic Response at Maintenance– Included Log-transformed Statistics | Same as above | W48, W96 |

## 13.13.12. 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 ≥50c/mL (yes vs. no) at Week 48 | For W96 delivery, replace Week 48 with Week 96 | W48, W96 |
| 5.2. | PK | Shell FPK01/Figure 11.1005 | Scatter Plot of Last Trough RPV PK Concentration by Snapshot HIV-1 RNA≥50 c/mL (yes vs. no) at Week 48 | For W96 delivery, replace Week 48 with Week 96 | W48, W96 |
| 5.3. | PK | Shell FPK01/Figure 11.1004 | Scatter Plot of Week 8 Trough CAB PK Concentration by Snapshot 'HIV-1 RNA≥50 c/mL' (yes vs. no) at Week 48 | For W96 delivery, replace Week 48 with Week 96 | W48, W96 |
| 5.4. | PK | Shell FPK01/Figure 11.1005 | Scatter Plot of Week 8 Trough RPV PK Concentration by Snapshot HIV-1 RNA≥50 c/mL (yes vs. no) at Week 48 | For W96 delivery, replace Week 48 with Week 96 | W48, W96 |
| 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)<br><br>For W96 delivery, replace Week 48 with Week 96 | W48, W96 |

| 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)<br><br>For W96 delivery, replace Week 48 with Week 96 | W48, W96 |
| 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) | For W96 delivery, replace Week 48 with Week 96 | W48, W96 |
| 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) | For W96 delivery, replace Week 48 with Week 96 | W48, W96 |
| 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. Induction Baseline BMI category will also be marked<br><br>For W96 delivery, replace Week 48 with Week 96 | W48, W96 |

| Pharmacokinetic / Pharmacodynamic: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** The similar outputs below from study 200056 (week48idsl) | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 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, W96 |
| **PK Concentration and safety measures** | | | | | |
| 5.11. | PK | shell FPK03 | Scatter Plot of Change from Maintenance Baseline (Day 1) in 2-Hr QTc versus CAB 2-Hr Post-dose PK Concentrations at Week 4b 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.<br>(2hr post dose PK concentration at WK4b, week 48 vs CFB in QTC at these two visits)<br><br>For W96 delivery, replace Week 48 with Week 96 | W48, W96 |
| 5.12. | PK | Shell FPK03 | Scatter Plot of Change from Maintenance Baseline (Day 1) in 2-Hr QTc versus RPV 2-Hr Post-dose PK Concentrations at Week4b and Week 48 | Similar to the above for CAB | W48, W96 |

| 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 Maintenance Baseline (Day 1) in ALT versus Last Trough CAB PK Concentrations during the 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 | W48, W96 |
| 5.14. | PK | shell FPK04 | Scatter Plot of Maximum Change from Maintenance Baseline (Day 1) in ALT versus Last Trough RPV PK Concentrations during the Maintenance Phase | Same as above for CAB | W48, W96 |
| 5.15. | PK | shell FPK04 | Scatter Plot of Maximum Change from Maintenance Baseline (Day 1) in Total Bilirubin versus Last Trough CAB PK Concentrations during the 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 | W48, W96 |
| 5.16. | PK | shell FPK04 | Scatter Plot of Maximum Change from Maintenance Baseline (Day 1) in Total Bilirubin versus Last Trough RPV PK Concentrations during the Maintenance Phase | Same as above for CAB | W48, W96 |
| 5.17. | PK | shell FPK05 | Box Plot of Maximum Toxicity Grades of Most Frequently Reported non-ISR AEs (e.g. Headache, Fever, Fatigue, Nausea, Dizziness) versus Last Trough CAB PK Concentrations during the Maintenance Phase | The AEs for this analysis should be the top 5 in incidence of non-ISR AEs within the Q4W arm during the Maintenance Phase. | W48, W96 |

| 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 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 during the 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 | |
| 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 during the Maintenance Phase | The same as above | W48, W96 |

## 13.13.13. Health Outcomes Tables

| Health Outcomes: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Perception of iNjection Questionnaire (PIN)** | | | | | |
| 6.1. | ITT-E | THO2 | Proportion of Subjects with each individual item score in PIN by Visit – LOCF (Maintenance Phase) | | W48, W96 |
| 6.2. | 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) | | W48, W96 |
| 6.3. | 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 (acceptance score only) | W48, W96 |
| 6.4. | 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) | | W48, W96 |
| 6.5. | 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) | | W48, W96 |
| **Health-related quality of Life (HATQoL)** | | | | | |
| 6.6. | ITT-E | THO2 | Proportion of Subjects with each Individual Questionnaire Item Score in HATQoL by Visit - LOCF (Maintenance Phase) | | W48, W96 |
| 6.7. | ITT-E | THO1 | Summary of Quality of Life (HATQoL) Score in Life Satisfaction, HIV Medication, and Disclosure worries by Visit (Maintenance | | W48, W96 |

| Health Outcomes: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| | | | Phase) | | |
| 6.8. | ITT-E | THO1 | Summary of Quality of Life (HATQoL) Score in Life Satisfaction, HIV medication, and Disclosure worries by Visit - LOCF (Maintenance Phase) | | W48, W96 |
| 6.9. | ITT-E | THO1 | Summary of Quality of Life Score (HATQoL) – Change from Maintenance Baseline (Day 1) in Life Satisfaction, HIV Medication, and Disclosure Worries by Visit (Maintenance Phase) | | W48, W96 |
| 6.10. | ITT-E | THO1 | Summary of Quality of Life Score (HATQoL) – Change from Maintenance Baseline (Day 1) in Life Satisfaction, HIV Medication, and Disclosure Worries by Visit - LOCF (Maintenance Phase) | | W48, W96 |
| 6.11. | ITT-E | Shell THO3 | Statistical Analysis of Quality of Life Score (HATQoL) – Change from Maintenance Baseline (Day 1) in Life Satisfaction, HIV medication, and Disclosure Worries by Visit – LOCF (Maintenance Phase) | ANCOVA for analysis | W48, W96 |
| **Health Status:12-item short form survey (SF-12)** | | | | | |
| 6.12. | ITT-E | THO2 | Proportion of Subjects with SF-12 Individual Item Scores by Visit - LOCF (Maintenance Phase) | | W48, W96 |
| 6.13. | ITT-E | THO1 | Summary of SF-12 (Total Score, MCS and PCS Scores) by Visit (Maintenance Phase) | | W48, W96 |
| 6.14. | ITT-E | THO1 | Summary of SF-12 (Total Score, MCS and PCS Scores) by Visit - LOCF (Maintenance Phase) | | W48, W96 |
| 6.15. | ITT-E | THO1 | Summary of Change from Maintenance Baseline (Day 1) in SF-12 (Total Score, MCS and PCS Scores) by Visit (Maintenance Phase) | | W48, W96 |
| 6.16. | ITT-E | THO1 | Summary of Change from Maintenance Baseline (Day 1) in SF- | | W48, W96 |

| Health Outcomes: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| | | | 12 (Total Score, MCS and PCS Scores) by Visit - LOCF (Maintenance Phase) | | |
| 6.17. | ITT-E | Shell THO3 | Statistical Analysis of SF-12 Change from Maintenance Baseline (Day 1) in Total Score, MCS, and PCS Score by Visit – LOCF (Maintenance Phase) | ANCOVA for analysis | W48, W96 |
| **Treatment Satisfaction (HIVTSQs)** | | | | | |
| 6.18. | ITT-E | Shell THO2 | Proportion of Subjects with HIVTSQs – Treatment Satisfaction Individual Item Scores by Visit - LOCF) (Maintenance Phase) | | W48, W96 |
| 6.19. | ITT-E | Shell THO2 | Proportion of Subjects with HIVTSQs – Treatment Satisfaction Individual Item Scores by Visit and Subgroup - LOCF) (Maintenance Phase) | Subgroups: Induction Baseline (Week -20) HIV-1 RNA (<100,000, ≥100,000 c/mL), gender at birth, age (<35; 35-<50; ≥50), Maintenance Baseline (Day 1) CD4+ cell count (<200; 200 to <350; 350 to <500; ≥ 500 cells/mm3), and race (i.e. white, non-white). | W48, W96 |
| 6.20. | ITT-E | Shell THO1 | Summary of HIVTSQs - Total Treatment Satisfaction Score by Visit) (Maintenance Phase) | | W48, W96 |
| 6.21. | ITT-E | Shell THO1 | Summary of HIVTSQs - Total Treatment Satisfaction Score by Visit - LOCF) (Maintenance Phase) | | W48, W96 |

| Health Outcomes: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 6.22. | ITT-E | Shell THO1 | Summary of HIVTSQs - Change from Maintenance Baseline (Day 1) in Total Treatment Satisfaction Score by Visit (Maintenance Phase) | | W48, W96 |
| 6.23. | ITT-E | Shell THO1 | Summary of HIVTSQs - Change from Maintenance Baseline in Total Treatment Satisfaction Score by Visit- LOCF (Maintenance Phase) | | W48, W96 |
| 6.24. | ITT-E | Shell THO3 | Statistical Analysis of HIVTSQs - Change from Maintenance Baseline (Day 1) in Total Treatment Satisfaction Score by Visit – - LOCF) (Maintenance Phase) | ANCOVA for analysis | W48, W96 |
| **Treatment Satisfaction (HIVTSQc)** | | | | | |
| 6.25. | ITT-E | Shell THO2 | Proportion of Subjects with HIV-Treatment Satisfaction Questionnaire Individual Item Scores change) (Maintenance Phase) | | W48, W96 |
| 6.26. | ITT-E | Shell THO1 | Summary of HIV-Treatment Satisfaction Questionnaire in Treatment Satisfaction Score Change) (Maintenance Phase) | | W48, W96 |
| 6.27. | ITT-E | Shell THO5 | Statistical Analysis of HIV-Treatment Satisfaction Questionnaire in Treatment Satisfaction Score Change at Week 48 (Maintenance Phase) | ANOVA for analysis | W48, W96 |
| **Treatment Acceptance (ACCEPT)** | | | | | |
| 6.28. | ITT-E | Shell THO2 | Proportion of Subjects with Treatment Acceptance Questionnaire (ACCEPT) Individual Item Scores by Visit - LOCF) (Maintenance Phase) | | W48, W96 |

| Health Outcomes: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 6.29. | ITT-E | Shell THO1 | Summary of Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit (Maintenance Phase) | | W48, W96 |
| 6.30. | ITT-E | Shell THO1 | Summary of Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit - LOCF (Maintenance Phase) | | W48, W96 |
| 6.31. | ITT-E | Shell THO1 | Summary of Change from Maintenance Baseline in Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit (Maintenance Phase) | | W48, W96 |
| 6.32. | ITT-E | Shell THO1 | Summary of Change from Maintenance Baseline in Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit - LOCF (Maintenance Phase) | | W48, W96 |
| 6.33. | ITT-E | Shell THO3 | Statistical Analysis of Change from Maintenance Baseline in Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit – LOCF (Maintenance Phase) | ANCOVA for analysis | W48, W96 |
| **Tolerability of Injection, NRS (for Q4W IM)** | | | | | |
| 6.34. | ITT-E | Shell THO2 | Proportion of Subjects with Tolerability of Injection (NRS) Individual item scores by Visit - LOCF) (Maintenance Phase) | | W48, W96 |
| 6.35. | ITT-E | Shell THO9 | Summary of Tolerability of Injection(NRS) scores by Visit (Maintenance Phase) | | W48, W96 |
| 6.36. | ITT-E | Shell THO9 | Summary of Tolerability of Injection(NRS) scores by Visit - LOCF) (Maintenance Phase) | | W48, W96 |
| 6.37. | ITT-E | Shell THO9 | Summary of Tolerability of Injection (NRS) by Visit - Change from Week 4b Scores) (Maintenance Phase) | | W48, W96 |
| 6.38. | ITT-E | Shell THO9 | Summary of Tolerability of Injection (NRS) by Visit - Change from Week 4b Scores - LOCF) (Maintenance Phase) | | W48, W96 |
| **Preferences (Dichotomous preference question) (for Q4W IM)** | | | | | |
| 6.39. | ITT-E | Shell THO8 | Treatment Preference at Week 48 (Maintenance Phase) | | W48 |

## 13.13.14. Health Outcomes Figures

| Health Outcomes: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 6.1. | ITT-E | Shell FHO1 | Line Plot of Adjusted Mean (95% CI) Change from Maintenance Baseline (Day 1) in HIVTSQs Total Treatment Satisfaction Score over Time(ANCOVA) -LOCF | | W48, W96 |
| 6.2. | ITT-E | Shell FHO2 | Line Plot of Difference (95% CI) in Adjusted Mean Change from Maintenance Baseline (Day 1) in HIVTSQs Total Treatment Satisfaction Score over Time(ANCOVA) -LOCF | | W48, W96 |
| 6.3. | ITT-E | Shell FHO1 | Line Plot of Adjusted Mean (95% CI) Change from Maintenance Baseline (Day 1) in SF-12 (Total, MCS and PCS subscale) Score over Time(ANCOVA) -LOCF | | W48, W96 |
| 6.4. | ITT-E | Shell FHO2 | Line Plot of Difference (95% CI) in Adjusted Mean Change from Maintenance Baseline (Day 1) in SF-12 (Total, MCS and PCS subscale) Score over Time (ANCOVA) -LOCF | | W48, W96 |
| 6.5. | ITT-E | Shell FHO1 | Line Plot of Adjusted Mean (95% CI) Change from Maintenance Baseline (Day 1) in HATQoL (Life Satisfaction, HIV medication, and Disclosure Worries) by Visit (ANCOVA) -LOCF | | W48, W96 |
| 6.6. | ITT-E | Shell FHO2 | Line Plot of Difference in Adjusted Mean (95% CI) Change from Maintenance Baseline (Day 1) in HATQoL (Life Satisfaction, HIV Medication, and Disclosure Worries) by Visit (ANCOVA) -LOCF | | W48, W96 |

## 13.13.15. Virology Tables

| Virology: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** (mock up below from study 200056\wk48idsl) | **Title** | **Programming Notes** | **Deliverable** |
| **Genotype** | | | | | |
| 7.1. | CVF | Table 9.1001 | Summary of the Prevalence of Known INI Resistance Mutations at time of CVF (Maintenance Phase) – Plasma Sample | 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' | W48, W96 |
| 7.2. | CVF | Table 9.1002 | Summary of the Prevalence of Treatment Emergent Known INI Resistance Mutations at time of CVF (Maintenance Phase) – Plasma Sample | 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' | W48, W96 |
| 7.3. | 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 | 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 | W48, W96 |

| Virology: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** (mock up below from study 200056\wk48idsl) | **Title** | **Programming Notes** | **Deliverable** |
| 7.4. | CVF | | Summary of the Prevalence of Treatment-Emergent Major Resistance Mutations of NRTI, NNRTI and PI Class at time of CVF (Maintenance Phase) - - Plasma Sample | 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 | W48, W96 |
| 7.5. | ITT-E | | Summary of the Prevalence of Major Resistance Mutations of NRTI, NNRTI and PI Class at Induction Baseline (Week -20) -- Plasma Sample | 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 | W48, W96 |
| **Phenotype** | | | | | |
| 7.6. | CVF | Table 9.1005 | Summary of Phenotype by Phenotypic Cutoff at time of CVF (Maintenance Phase) - - Plasma Sample | | W48, W96 |
| 7.7. | CVF | Table 9.1005 | Summary of Genotypic Susceptibility at time of CVF (Maintenance Phase) - - Plasma Sample | | W48, W96 |

| Virology: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** (mock up below from study 200056\wk48idsl) | **Title** | **Programming Notes** | **Deliverable** |
| 7.8. | CVF | Table 9.1005 | Summary of Net Assessment at time of CVF (Maintenance Phase) - Plasma Sample | | W48, W96 |
| 7.9. | CVF | Table 9.1006 | Summary of Phenotype: Number of Drugs to Which Subject are Resistant at Time of CVF (Maintenance Phase) - Plasma Sample | | W48, W96 |
| 7.10. | CVF | Table 9.1007 | Summary of Fold Change to CAB, RPV and DTG at Induction Baseline (Week -20) and Time of CVF (Maintenance Phase) - Plasma Sample | | W48, W96 |
| 7.11. | CVF | Table 9.1008 | Summary of Change from Induction Baseline (Week -20) in Fold Change to CAB, RPV, and DTG (Maintenance Period) | | W48, W96 |
| 7.12. | CVF | Shell TV1 | Summary of Viral load, Genotypic and Phenotypic data for Subjects Who Met Confirmed Virologic Failure Criteria During the Maintenance Phase – Induction Baseline (Week -20) and Time of CVF | | HL, W48, W96 |
| 7.13. | CVF | Shell TV1 | Summary of Viral load, Genotypic and Phenotypic data for Subjects Who Met Confirmed Virologic Failure Criteria During the Extension Phase | | W96, EOS |
| 7.14. | ITT-E | Shell TV1 | Summary of Viral load, Genotypic and Phenotypic data for Non-CVF Subjects | May include genotypic and phenotypic data on the last on-treatment isolates for participants with HIV-1 RNA ≥200 c/mL | W48, W96, 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) | W48, W96, EOS |
| 2. | Randomised | TA1 | Listing of Randomised and Actual Strata and Treatment Assignment | CS CORE | W48, W96, EOS |
| 3. | All Subjects Screened | ES7 | Listing of Reasons for Screen Failure | CS CORE | W48, W96, EOS |
| 4. | ITT-E | ES2 | Listing of Reasons for Study Withdrawal | CS CORE | HL, W48, W96, EOS |
| 5. | ITT-E | ES2 | Listing of Reasons for Study Drug Discontinuation | CS CORE | W48, W96, EOS |
| 6. | All Enrolled | DV2 | Listing of Important Protocol Deviations | CS CORE | W48, W96, EOS |
| 7. | ITT-E | DV2 | Listing of Protocol Deviations Leading to Exclusion from the Per-Protocol Population | CS CORE | HL, W48, W96, EOS |
| 8. | All Enrolled | IE3 | Listing of Subjects with Inclusion/Exclusion Criteria Deviations | CS CORE | W48, W96, EOS |
| 9. | ITT-E | DM2 | Listing of Demographic Characteristics | CS CORE | W48, W96, EOS |
| 10. | ITT-E | DM9 | Listing of Race | CS CORE | W48, W96, EOS |
| **Primary Efficacy** | | | | | |
| 11. | ITT-E | Shell LPEF1 | Listing of Study Outcome (50 c/mL) at Week 48 – Snapshot Analysis | | HL, W48, W96, EOS |
| **Exposure** | | | | | |
| 12. | Safety | HIV_IP5 | Listing of Investigational Product Exposure Data | CS CORE | W48, W96, EOS |

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **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 | W48, W96, EOS |
| 14. | Safety | AE14 | Listing of Reasons for Considering as a Serious Adverse Event (Maintenance +Extension Phase) | CS CORE | W48, W96, EOS |
| 15. | Safety | AE8 | Listing of Fatal Adverse Events (Maintenance +Extension Phase) | CS CORE | W48, W96, EOS |
| 16. | All Enrolled | AE8 | Listing of Non-Fatal Serious Adverse Events (Induction Phase) | CS CORE | W48, W96, EOS |
| 17. | Safety | AE8 | Listing of Non-Fatal Serious Adverse Events (Maintenance +Extension Phase) | CS CORE | W48, W96, EOS |
| 18. | All Enrolled | AE8 | Listing of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product (Induction Phase) | CS CORE | W48, W96, EOS |
| 19. | Safety | AE8 | Listing of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product (Maintenance +Extension Phase) | CS CORE | HL, W48, W96, EOS |
| 20. | Safety | AE8 | Listing of changes in intensity/grades of Injection Site Related AE (Maintenance +Extension Phase) | Based on AE details inform page for changes in intensity of the same event. | W48, W96, EOS |
| 21. | Safety | PREG1a | Listing of Subjects Who Became Pregnant During the Study (Maintenance +Extension Phase) | | W48, W96, EOS |
| **Laboratory** | | | | | |
| **Hepatobiliary (Liver)** | | | | | |
| 22. | Safety | MH2 | Listing of Medical Conditions for Subjects with Liver stopping Events | | W48, W96, EOS |
| 23. | Safety | SU2 | Listing of Substance Use for Subjects with Liver Stopping Events | | W48, W96, EOS |

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **ECG & Vital Signs** | | | | | |
| 24. | Safety | EG3 | Listing of ECG Values for subjects with a value of potential clinical importance | | W48, W96, EOS |
| 25. | Safety | EG5 | Listing of ECG Findings | | W48, W96, EOS |
| **eC-SSRS** | | | | | |
| 26. | Safety | PSRAE1 | Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Section 1-Section 2) | | W48, W96, EOS |
| 27. | Safety | PSRAE3 | Listing of Possible Suicidality-Related Adverse Event Data: Possible Cause(s) (Section 3) | | W48, W96, EOS |
| 28. | Safety | PSRAE4 | Listing of Possible Suicidality-Related Adverse Event Data (Section 4) | | W48, W96, EOS |
| 29. | Safety | PSRAE5 | Listing of Possible Suicidality-Related Adverse Event Data (Section 5-Section 8) | | W48, W96, EOS |
| PK | | | | | |
| 30. | PK pop | Study 200056 Listing 10.1001(wk48idsl) | Listing of Plasma CAB PK Concentration-Time Data | Add a variable of 'evaluable' (Y/N) | W48, W96, EOS |
| 31. | PK pop | Study 200056 Listing 10.1002(wk48idsl) | Listing of Plasma RPV PK Concentration-Time Data | Add a variable of 'evaluable' (Y/N) | W48, W96, EOS |

## 13.13.17. Non-ICH Listings

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Study Population** | | | | | |
| 32. | All Enrolled | ES2 | Listing of Reasons for Induction Phase Withdrawal | | W48, W96, EOS |
| 33. | ITT-E | ES2 | Listing of Reasons for Maintenance Phase Withdrawal | | W48, W96, EOS |
| 34. | ITT-E | ES2 | Listing of Reasons for Oral Lead-in Period Withdrawal | | W48, W96, EOS |
| 35. | ES | ES2 | Listing of Reasons for Extension Phase Withdrawal | | W96, EOS |
| 36. | LTFU | ES2 | Listing of Reasons for Long-term Follow Up Withdrawal | | W48, W96, EOS |
| 37. | All Enrolled | CA3 | Listing of Prior ART Medications | | W48, W96, EOS |
| 38. | All Enrolled | CA3 | Listing of Concomitant ART Medications Received during Induction Phase | | WK48, W96, EOS |
| 39. | ITT-E | CA3 | Listing of Concomitant ART Medications Received during Maintenance Phase | | W48, W96, EOS |
| 40. | ITT-E | CA3 | Listing of ART Medications Received during LTFU Phase | | W48, W96, EOS |
| 41. | ITT-E | CA3 | Listing of subjects with changes in Concomitant ARTs during Maintenance Phase | | W48, W96, EOS |
| 42. | ITT-E | Shell LSP11 | Listing of Investigational Product Accountability - Oral Regimens | | W48, W96, EOS |
| 43. | ITT-E | MHSZE | Listing of Medical History of Seizure | | W48, W96, EOS |
| **Secondary Efficacy** | | | | | |
| 44. | All Enrolled | Shell LSEF3 | Listing of All Plasma HIV-1 RNA data for subjects with Confirmed Virologic Failure (Induction Phase) | | W48, W96, EOS |
| 45. | CVF | Shell LSEF3 | Listing of All Plasma HIV-1 RNA data for subjects with Confirmed Virologic Failure | | W48, W96, EOS |

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 46. | ITT-E | Shell LSEF1 | Listing of All Plasma HIV-1 RNA data for subjects with viral load >=50 c/mL at any time during the Maintenance Phase | | HL, W48, W96, EOS |
| 47. | ITT-E | Shell LSEF1 | Listing of Plasma All HIV-1 RNA data for subjects with viral load >=50 c/mL during the Maintenance Oral lead-in Period | | W48 |
| 48. | ITT-E | Shell LSEF5 | Listing of HIV-1 Associated Conditions | | W48, W96, EOS |
| **Safety (The Safety listings below list data for Maintenance + Extension Phases, unless otherwise specified)** | | | | | |
| 49. | Safety | ABC_HSR _EXPO2 | Listing of Abacavir Hypersensitivity Reaction Record - Exposure to Abacavir | | W48, W96, EOS |
| 50. | Safety | ABC_HSR _DRUG2 | Listing of Abacavir Hypersensitivity Reaction Record - Subject History of Drug Allergies | | W48, W96, EOS |
| 51. | Safety | ABC_HSR COND2 | Listing of Abacavir Hypersensitivity Reaction Record - Subject and Family Conditions | | W48, W96, EOS |
| 52. | Safety | ABC_HSR _RASH2 | Listing of Abacavir Hypersensitivity Reaction Record - Skin Rash Details | | W48, W96, EOS |
| 53. | Safety | ABC_HSR _SYMP4 | Listing of Abacavir Hypersensitivity Reaction Record - Symptoms | | W48, W96, EOS |
| 54. | Safety | VS4 | Listing of Abacavir Hypersensitivity Reaction Record - Vital Signs | | W48, W96, EOS |
| 55. | Safety | ABC_HSR _SYMP6 | Listing of Abacavir Hypersensitivity Reaction Record - Individual Symptoms and Diagnostic Category Assignments (Excluding Other Symptoms) | | W48, W96, EOS |
| 56. | Safety | ABC_HSR _SYMP7 | Listing of Abacavir Hypersensitivity Reaction Record - Individual Symptoms and Diagnostic Category Assignments (Other Symptoms) | | W48, W96, EOS |
| 57. | Safety | LIVER5 | Listing of Liver monitoring/stopping Event reporting | | W48, W96, EOS |
| 58. | Safety | LIVER6 | Listing of Liver Event Information for RUCAM Score | | W48, W96, EOS |
| 59. | Safety | LIVER7 | Listing of Liver Biopsy Details | | W48, W96, EOS |

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / TST ID / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 60. | Safety | LIVER8 | Listing of Liver Imaging Details | | W48, W96, EOS |
| 61. | Safety | Liver13 | Listing Subjects Meeting Hepatobiliary Lab Criteria (Maintenance + Extension 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) | W48, W96, EOS |
| 62. | Safety | AE8 | Listing of Adverse Events Potentially Related to Torsades de Pointe | | W48, W96, EOS |
| 63. | Safety | EG3 | Listing of ECG values for subjects with Adverse Events Potentially Related to Torsades de Pointes | | W48, W96, EOS |
| 64. | 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) | HL, W48, W96, EOS |
| 65. | Safety | Latte2 WK96CDISC report | Listing of Investigational Product Exposure Data for Subject Receiving Oral Bridging | 8.1038 | W48, W96, EOS |
| 66. | Safety | DEV1 | Listing of Dosing Errors and IP Device Malfunctions | | W48, W96, EOS |
| **Virology (mock up below from study 200056\wk96cdisc), 'Study Phase' will be added as a column to the listing.** | | | | | |
| 67. | CVF | Listing 9.1005 | Listing of Replication Capacity in IN and PR/RT Region | | W48, W96, 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. See full details of the analysis and decision criteria in the IDMC charter.

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 were provided in a separate critical components RAP.

### 13.14.1. CVF Monitoring (Adhoc IDMC review)

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

The Statistics Data Analysis Centre (SDAC) is 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).

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

| Programming Instructions for the Kaplan-Meier analysis of treatment-related discontinuation equals failure (TRDF) | | |
|---|---|---|
| **Condition** | **Censor Status** | **Event Description/AVAL** |
| 1. Participant met CVF event criteria during the Maintenance Phase (based on derived CVF) | CNSR=0 | EVNTDESC=CVF<br>AVAL=Date of SVF*<br>*immediately preceding CVF |
| 2. Participant with Maintenance Phase withdrawal due to *'Lack of Efficacy', 'Treatment related AE', 'intolerability due to injection',* or *'protocol defined Safety stopping criteria'* during Maintenance Phase<br><br>Note: primary reason for discontinuation based on Maintenance Conclusion form in the eCRF. 'Treatment related AE' is defined as subjects that have primary reason for withdrawal =AE and that the participant has at least one AE considered drug related and leading to withdrawal/permanent discontinuation of investigational product. | CNSR=0 | EVNTDESC= terms in italic, respectively.<br><br>For ABC/DTG/3TC arm:<br>AVAL= min [Study Day of Maintenance Phase Discontinuation, Study Day of Maintenance IP Stop Date + 1]<br><br>For Q4W arm:<br>AVAL= min [Study Day of Maintenance Phase Discontinuation, max(Study Day of Last Q4W IM Dose + 35, Study Day of Last Oral CAB/RPV Dose + 1)]<br><br>Note: Last Q4W IM / last oral dose/ Maintenance IP Stop Date is only applied to subjects who permanently discontinue from study treatment.<br><br>Note: Date of Maintenance Phase discontinuation is from the Maintenance Phase Conclusion form in the eCRF. |
| **If none of the above conditions met** | | |
| 3. Participant with Maintenance Phase withdrawal due to other reasons | CNSR=1 | EVNTDESC='Censored due to Study Discontinuation for Other Reasons'<br><br>AVAL will be defined as the same as above 2 |
| 4. Participant did not have premature withdrawal from the Maintenance Phase | CNSR=1 | EVNTDESC='Censored due to data cutoff for analysis'<br><br>AVAL = Last on-treatment date during the Maintenance Phase,<br><br>For ABC/DTG/3TC arm: |

| Programming Instructions for the Kaplan-Meier analysis of treatment-related discontinuation equals failure (TRDF) | | |
|---|---|---|
| **Condition** | **Censor Status** | **Event Description/AVAL** |
| | | min [Study Day of Week 100 Visit, Day of Last Contact at time of analysis, Study Day of Maintenance IP stop Date + 1]<br><br>For Q4W arm<br>min [Study Day of Week 100 Visit, Study Day of Starting LTFU HAART, Study Day of Last Contact Date at time of analysis, max(Study Day of Last Q4W IM Dose + 35, Study Day of Last oral CAB/RPV dose + 1)] |

The same approach as will be used to define 'ERDF', Efficacy-related discontinuation equals failure, 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.