Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)
Title	:	Reporting and Analysis Plan for Protocol 207966: Study Evaluating the Efficacy, Safety, and Tolerability of Long-acting Cabotegravir Plus Long-acting Rilpivirine administered every 8 weeks in Virologically Suppressed HIV-1-infected Adults
Compound Number	:	GSK1265744
Effective Date	:	17-JAN-2019

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 207966
- This RAP will be provided to the study team members to convey the content of the Week 24/Week 48/Week 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:

Revision Chronology:		
2017N326521_00	17-JUL-2017	Original
2017N326521_01	14-SEP-2017	The primary purpose of protocol amendment # 1 is to revise the study sample size to randomize approximately 1020 participants including 510 participants per arm based on a non-inferiority margin of 4% between the CAB LA + RPV LA Q8W and Q4W arms.
2017N326521_02	03-Jul-2018	The primary reasons for amendment #2 are to: • Add the additional interim analysis of data when all subjects have completed the Week 24 visit, with the intent of expediting the submission of study results to Health Authorities; • Change the objective for assessing the preference for CAB LA + RPV LA every 8 weeks or CAB LA + RPV LA every 4 weeks LA compared to oral antiretroviral (ARV) and the preference for CAB LA+ RPV LA every 8 weeks compared to CAB LA + RPV LA every 4 weeks from an exploratory objective to a secondary objective. A change to the supporting version of the Preference questionnaire administered to participants at Week 48 (or withdrawal) is also acknowledged; • Add revisions and clarifications for the administration of health outcomes questionnaires; • Extend exclusion criterion #28 to also exclude hereditary coagulation and platelet disorders such as haemophilia or Von Willebrand Disease; • Update exclusion criterion #11 to indicate that CD4+ counts <200 cells/µL are not exclusionary; • Offer clarification that withdrawal assessments will be performed for any participant who withdraws prematurely from the Maintenance or Extension Phase. Additional guidance for participants withdrawing at Week 52 or Week 100 has been added; • Offer guidance to monitor medications that are dependent on OAT1 and OAT3 transport upon concomitant exposure with CAB; • Specify that 2-hour post-dose ECG should be performed at Day 1 and Week 48 only for participants receiving CAB LA + RPV LA as it is not required to perform 2-hour post-dose ECG for those receiving oral CAB + RPV at Day 1;

Revision Chronology:		
		• Exclude language that previously indicated hormonal contraception may be susceptible to interaction with the study drugs. The lack of a demonstrated interaction with a representative contraceptive supports use of CAB and RPV across a broad range of estrogen and progestin or progestin only hormonal contraceptives; • Add minor clarifications and corrections to typographical errors/formatting to protocol text.

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 amendment 2 [(Dated: 03/JUL/2018)].

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

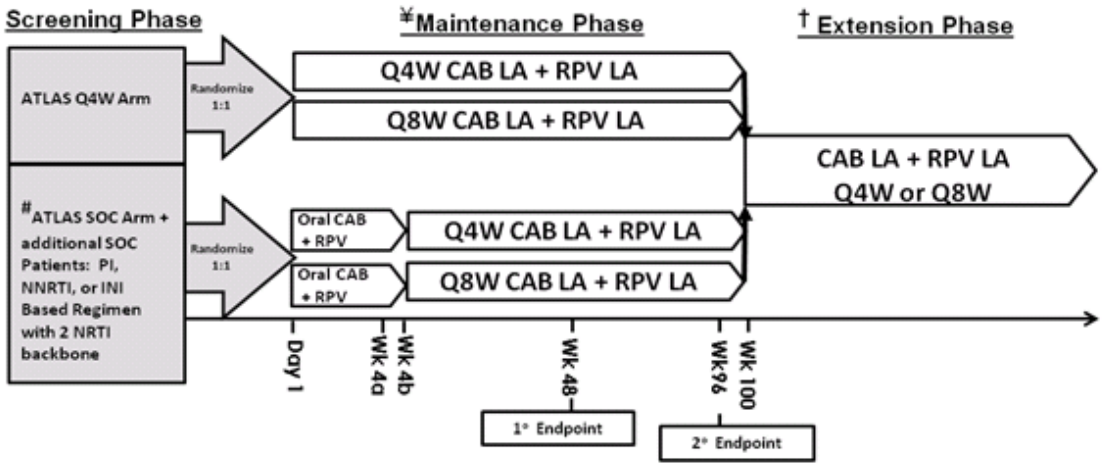
Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To demonstrate the non-inferior antiviral activity of CAB LA + RPV LA every 8 weeks (every two months) compared to CAB LA + RPV LA every 4 weeks (monthly) over 48 weeks in suppressed HIV-1 infected antiretroviral therapy (ART)-experienced participants	• 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)
Secondary Objectives	**Secondary Endpoints**
• To demonstrate the antiviral and immunologic activity of CAB LA + RPV LA every 8 weeks compared to CAB LA + RPV LA every 4 weeks	• Proportion of participants with plasma HIV-1 RNA <50 c/mL (c/mL) at Week 24, Week 48 and Week 96 using the FDA Snapshot algorithm (Intent-to-Treat Exposed [ITT-E] population) • Proportion of participants with protocol-defined confirmed virologic failure (CVF) through Week 24, Week 48 and Week 96 • Proportion of participants with HIV-RNA greater than or equal to 50 c/mL as per FDA Snapshot algorithm at Week 24 and Week 96 • Absolute values and changes from Baseline in viral load and CD4+ cell counts over time including Week 48 and Week 96
• To evaluate the safety and tolerability of CAB LA + RPV LA every 8 weeks compared to CAB LA + RPV LA every 4 weeks	• Incidence and severity of AEs and laboratory abnormalities over time including Week 24, Week 48 and Week 96 • Proportion of participants who discontinue treatment due to AEs over time including Week 24, Week 48 and Week

Objectives	Endpoints
	96 • Change from Baseline in laboratory parameters over time including Week 48 and Week 96
• To assess viral resistance in participants experiencing protocol-defined confirmed virologic failure	• Incidence of treatment emergent genotypic and phenotypic resistance to CAB, RPV through Week 24, Week 48 and Week 96
• To characterize CAB and RPV concentrations and population pharmacokinetics and identify important determinants of variability	• Plasma PK parameters for CAB LA and RPV LA (when evaluable, Ctrough, concentrations post dose [~Cmax], and area under the curve [AUC]) • Demographic parameters including, but not limited to, age, sex, race, body weight, body mass index, and relevant laboratory parameters will be evaluated as potential predictors of inter- and intra-participant variability for pharmacokinetic parameters
• To assess preference for CAB LA + RPV LA every 8 weeks or CAB LA + RPV LA every 4 weeks LA compared to oral antiretroviral (ARV) • To assess preference for CAB LA+ RPV LA every 8 weeks compared to CAB LA + RPV LA every 4 weeks	• Preference for CAB LA + RPV LA every 8 weeks and CAB LA + RPV LA every 4 weeks compared to oral ARV and preference for CAB LA + RPV LA every 8 weeks compared to CAB LA + RPV LA every 4 weeks will be assessed using a preference questionnaire at week 48 (or Withdrawal).
• To assess patient reported health-related quality of life, treatment satisfaction, injection tolerability, and treatment acceptance.	• Change from Baseline (Day 1) in HRQoL at Week 24, and Week 48 (or Withdrawal) • Change from baseline (Day 1) in total "treatment satisfaction" score, and individual item scores of the HIV Treatment Satisfaction Status Questionnaire (HIVTSQs) at Week 24, and 48, (or Withdrawal) • Change in treatment satisfaction over time using the HIV Treatment Satisfaction Change Questionnaire HIVTSQc at Week 48 (or Withdrawal). • Change from Week 8 in Dimension scores ("CCI [redacted]", and "CCI [redacted]") 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 will be assessed using the Perception of Injection questionnaire (PIN) at Weeks 24, and 48 (or Withdrawal) • Change from Baseline (Day 1) in treatment acceptance at Week 24 and Week 48 (or Withdrawal) will be assessed using the "General acceptance" dimension of the Chronic Treatment Acceptance (ACCEPT) questionnaire
Exploratory Objectives	**Exploratory Endpoints**
• 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 <50 c/mL over time • Proportion of participants with confirmed virologic failure over time • Incidence of treatment emergent genotypic and phenotypic resistance to CAB and RPV in over time • Incidence and severity of AEs and laboratory

Objectives	Endpoints
	abnormalities over time • Proportion of participants who discontinue treatment due to AEs over time • Absolute values and changes in laboratory parameters over time • Incidence of disease progression (HIV-associated conditions, acquired immunodeficiency syndrome [AIDS] and death)
• To explore the effect of patient characteristics on virologic and immunologic responses to CAB LA+ RPV LA every 8 weeks compared to CAB LA + RPV LA every 4 weeks	• Proportion of participants by patient subgroup(s) (e.g., by age, gender, BMI, race, HIV-1 subtype, Baseline CD4+, type of oral treatment [NNRTI, PI, or INSTI], duration prior CAB LA and RPV LA exposure [0 weeks, 1-24 weeks, > 24 weeks]) with HIV-RNA greater than or equal to 50 c/mL, and with protocol-defined confirmed virologic failure over time including Week 48 and Week 96 using the Snapshot algorithm for the ITT-E population • Change from Baseline in CD4+ cell counts 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 CAB and RPV concentrations and virologic, immunologic responses, and/or occurrence of adverse events [AEs] over time.
• To assess reason for switching using a single question. • To assess reason for continuation using a single question	• For patients randomized from oral SOC, the reasons for willingness to switch ART at baseline (Day 1) will be assessed • For patients randomized from CAB LA + RPV LA every 4 weeks in ATLAS, the reasons for willingness to continue long-acting ART at baseline (Day 1) will be assessed

2.3. Study Design

Overview of Study Design and Key Features



N=1020, randomized 1:1 to each arm and stratified by prior CAB+RPV Exposure
# SOC Patients not transitioning from the ATLAS study must be on uninterrupted current regimen (either the initial or second cART regimen) for at least 6 months prior to Screening. Documented evidence of at least two plasma HIV-1 RNA measurements <50 c/mL in the 12 months prior to Screening: one within the 6 to 12 month window, and one within 6 months prior to Screening. No history of virologic failure. No evidence of viral resistance based on the presence of any resistance-associated major INI, or NNRTI mutation (except K103N) from prior genotype assay results. No current or prior history of etravirine use.
†Optional Extension Phase to continue randomized CAB LA + RPV LA Q4W or Q8W at Wk 100
¥Participants who withdraw from IM arm must go into 52 week long term follow up phase if randomized regimen is not yet locally approved and commercially available.

Design Features	• Study 207966 (Antiretroviral Therapy as Long Acting Suppression every 2 Months-ATLAS-2M) is a Phase IIIb, randomized, open-label, active-controlled, multicenter, parallel-group, non-inferiority study designed to assess the antiviral activity and safety of CAB LA + RPV LA administered every 4 weeks compared CAB LA + RPV LA administered every 8 weeks in approximately 1020 adult HIV-1 infected patients.
	• The ATLAS-2M study comprises a Screening Phase (up to 35 days), and a Maintenance Phase (Day 1 to Week 100), followed by an Extension Phase (post Week 96). 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 52 weeks after the last dose of CAB LA and/or RPV LA, or until the assigned CAB LA + RPV LA regimen is locally approved and commercially available.
	• Two groups of patients who fulfill eligibility requirements will be randomized (1:1) at Day 1 to receive CAB LA + RPV LA Q4W, or CAB LA + RPV LA Q8W regimen for at least 100 weeks:
	  • Group 1: Patients randomized from current ART Standard of Care (SOC) therapy
	  • Group 2: Patients currently receiving CAB LA + RPV LA Q4W

Dosing	• Group 1: oral therapy with CAB 30 mg + RPV 25 mg once daily at Day 1 for 28 days (±3 days) to determine individual safety and tolerability, followed by CAB LA + RPV LA Q4W or CAB LA + RPV LA Q8W (as randomized at Day 1) • Group 2: CAB LA + RPV LA Q4W or CAB LA + RPV LA Q8W (as randomized at Day 1)
Time & Events	• Refer to Appendix 2: Schedule of Activities

Overview of Study Design and Key Features	
Treatment Assignment	• Randomized (1:1) at Day 1 to receive CAB LA + RPV LA Q4W or CAB LA + RPV LA Q8W • GSK RandAll NG used to generate randomization schedules • Stratified Randomization by prior CAB+RPV exposure (0 weeks, 1 to 24 weeks, >24 weeks)
Interim Analysis	• Futility analysis at (approx.) 50% of subjects completing Week 24 • Continuous time monitoring of confirmed virologic failure (CVF) in the Q8W randomized arm until all participants complete Week 24 visit • The main analysis will be conducted to evaluate the primary objective of the protocol at Week 48. • Preliminary analyses at Week 24 and analyses at Week 96 • Further data cuts and analyses may be conducted as necessary in order to support regulatory submissions and publications.

2.4. Statistical Hypotheses / Statistical Analyses

The study is designed to demonstrate that the antiviral effect of Q8W dosing with CAB LA + RPV LA is non-inferior to Q4W dosing CAB LA + RPV LA in subjects stably suppressed on an oral SOC regimen or Q4W CAB LA + RPV LA regimen prior to randomization. Non-inferiority in the proportion of participants with HIV-1 RNA ≥50 c/mL at Week 48 (defined by the US FDA snapshot algorithm) can be concluded if the upper bound of a two-sided 95% confidence interval for the difference between the two treatment arms (Q8W – Q4W) is less than 4%.

If f_{Q8W} is the snapshot failure rate for Q8W CAB LA + RPV LA, and f_{Q4W} is the snapshot failure rate for Q4W CAB LA + RPV LA then the null (H_0) and alternative (Ha) hypotheses can be written as follows:

$$H_o: f_{Q8W} - f_{Q4W} \geq 4\% \textit{ vs } H_a: f_{Q8W} - f_{Q4W} < 4\%$$

3. PLANNED ANALYSES

Analyses will be conducted to support Independent Data Monitoring Committee (IDMC) review of study data. At least three analyses will be conducted to evaluate the objectives of the protocol after all subjects have completed their visits at Week 24, Week 48 and Week 96, respectively. Prior to Week 48 analysis complete, the Week 24 results will be restricted to only those study team members and GSK/ViiV Healthcare senior management who need to be involved in the analysis and interpretation of the results for reporting to regulatory authorities. Details on protection against operation bias for Week 48 analysis are documented in the Study Results Dissemination Plan (SRDP) for this study. There is no planned hypothesis testing on the treatment difference at Week 24 and no decisions will be made based on the Week 24 results. Details of the planned displays for Week 24 analyses are provided in Section 15.14.4. Further data cuts and analyses may be conducted as necessary in order to support regulatory submissions and publications (first publication at Week 48). The Week 48 analysis will be primary and no results will be shared publicly until Week 48 analysis is complete. A final End-of-Study analysis will be conducted when all subjects have completed the study.

3.1. IDMC Analyses

An IDMC will be instituted to ensure external objective medical and/or statistical review of efficacy and safety to protect the ethical interests and well-being of subjects and to protect the scientific validity of this study.

The IDMC will evaluate accumulating efficacy, tolerability, safety and PK of CAB LA + RPV LA Q8W during the study. An interim futility analysis will be performed for the IDMC to evaluate the efficacy of CAB LA + RPV LA Q8W prior to the final analyses.

The 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 the CAB LA + RPV LA Q8W injectable regimen demonstrates non-inferiority to the CAB LA + RPV LA Q4W regimen at Week 24, 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 (CVF) criteria before all subjects have completed Week 24 to ensure that subjects are not being sub-optimally treated in the CAB LA + RPV LA Q8W 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.

A list of outputs required for each IDMC analysis will be provided in the IDMC Charter. Data handing methods and derived data definitions will be the same as detailed in this RAP, unless otherwise stated.

3.2. Final Analyses

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

1. All subjects have completed Week 48 and had a re-test for HIV-1 RNA if necessary.
2. All required database cleaning activities have been completed and database release (DBR) and database freeze (DBF) has been declared by Data Management.
3. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed according to Ramos NG procedures.

Two secondary analyses will be conducted at Week 24 and Week 96 and a final End-of-Study analysis will be conducted when all subjects have completed the study as defined in the protocol.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• Comprised of all subjects screened for inclusion in the study. • Subjects may be re-screened once, for which they will receive a new subject number. • For disposition displays, except for the listing of subjects who were rescreened, only the latest re-screening data will be included. All screening data will be summarized or listed for other displays.	• Study Population
Randomized	• All subjects who were randomly assigned to treatment in the study. • In this study, the randomized population includes all enrolled participants, i.e. the randomized population is equivalent to the enrolled population. • This population will be based on the treatment the participant was randomized to.	• Study Population
Safety	• All randomized subjects who received at least one dose of study treatment. • Participants will be assessed according to actual treatment received.	• Safety
Intent-to-Treat Exposed (ITT-E)	• All randomized subjects who received at least one dose of study treatment. • Subjects will be assessed according to their randomized treatment, regardless of the treatment they received.	• Study Population • Efficacy • Health Outcomes
Per-Protocol (PP)	• All subjects in the ITT-E population with the exception of major protocol violators. • Protocol deviations that would exclude participants from the PP population are defined in Section 4.1 (Protocol Deviations) and Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population).	• Efficacy (Sensitivity Analysis)

Population	Definition / Criteria	Analyses Evaluated
Pharmacokinetic (PK)	• All subjects who received CAB and / or RPV and underwent PK sampling during the study and provide at least 1 non-missing CAB and / or RPV plasma concentration value (Non-quantifiable [NQ] values will be considered as non-missing values).	• PK
Confirmed Virologic Failure (CVF)	• All subjects in the ITT-E population who met Confirmed Virologic Failure (CVF) criteria.	• Virology • Efficacy
Long-term Follow-up (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 either at least one Long-term Follow-up phase clinic visit (i.e. have at least one long-term follow-up visit shown in the study database, LTFU month 1, LTFU month 3, etc) or have filled out the LTFU phase conclusion form.	• Safety • Study Population
Week 24 Futility	• All subjects 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 subjects who withdrew early but would have reached Week 24) • The IDMC cut-off date is the predicted Week 24 visit date (Last Subject Last Visit) corresponding to the time at which approximately 50% of subjects have completed Week 24.	• IDMC Futility Analysis (i.e. IDMC Week 24 Analyses)
Oral Lead-in	• All subjects who received at least one dose of study treatment during the oral lead-in period in ATLAS-2M study.	• Safety • Study Population • Efficacy
Q4W ATLAS	• All subjects in the ITT-E population who were randomized to Q4W arm in ATLAS.	• Health Outcomes
SOC	• All subjects in the ITT-E population who either were randomized to SOC arm in ATLAS or did not participate in ATLAS.	• Health Outcomes

Refer to Section 15.14: List of Data Displays which details the population used for each display.

4.1. Protocol Deviations

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

Important deviations which result in exclusion from the analysis population will also be summarised and listed. (Please refer to Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population).

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

- Data will be reviewed prior to freezing the database to ensure all important deviations and deviations which may lead to exclusion from the analysis are captured and categorised on the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of protocol deviations.

A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG Randomization System		Data Displays for Reporting	
Code	Description	Description	Order in TLF
A	Q8W	Q8W	1
B	Q4W	Q4W	2
C/A	Oral followed by Q8W	Q8W	1
C/B	Oral followed by Q4W	Q4W	2

Notes:

- Unless stated otherwise, data displays will present two treatment group columns (Q8W and Q4W), where treatment sequence C/A is pooled with sequence A and treatment sequence C/B is pooled with sequence B. The detailed treatment sequence descriptors (i.e. C/A and C/B) may be used in selected data listings. Treatment C refers to oral CAB + oral RPV, used for oral lead-in for subjects entering the study with no prior CAB+RPV exposure.

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

1. Q8W vs Q4W

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-treatment (see Table 8) assessment with a non-missing value, including those from unscheduled visits. 'Pre-treatment' here refers to prior to the study treatment (i.e. CAB and/or RPV) in this study.

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

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

5.3. Multicentre Studies

Data will be summarized for all centres combined. Country will be treated as an exploratory subgroup for analyses of the primary efficacy endpoint as described in Section 7.1.5.1 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: For the proportion of participants with plasma HIV-1 RNA ≥ 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 prior exposure to CAB+RPV (0 weeks, 1-24 weeks, >24 weeks). 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. See Section 7.1.5.1 for additional details on the statistical analysis methodology.
Other Subgroups / Covariates	See details in Section 5.4.2

5.4.2. Examination of Subgroups

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

- If the percentage of subjects is small within a particular subgroup, then the subgroup categories may be combined prior to un-blinding 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, 2014), 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 randomization strata, key demographic factors, Baseline CD4, CDC stage will be fall into this category. For these factors, subgroup analyses will be performed but likely underpowered so that a formal proof of efficacy will not be available individually

in all subgroups. If consistent findings across multiple comparisons were observed then these analyses would still be suggestive of a generalizable finding from the overall population.

EMA Subgroup Guideline Category 3: Factor with good argumentation why homogeneity of response to treatment is plausible. The impact of factors falling into this category will be explored.

- Additional covariates of clinical interest may also be considered.

Category	Covariates and / or Subgroups
EMA Subgroup Category 2:	
Randomization Strata	• Prior exposure to CAB+RPV (0 weeks, 1-24 weeks, >24 weeks) For analysis purposes, randomization strata will be rederived using eCRF data, even if this differs from the strata captured in RAMOS NG. All statistical analyses will adjust for the above randomization strata, unless stated otherwise. Treatment-by-Strata interactions will be assessed as specified in the analysis sections.
Demographic and Baseline Characteristic Subgroups	• Age: o < 35, 35 - < 50, ≥ 50 For the statistical modelling, '< 35' and '35 - < 50' will be consolidated i.e. the following age group will be used: o < 50, ≥ 50 For the summary of demographic characteristics, the following age groups will also be presented: o ≤ 18, 19 - 64, ≥ 65 (FDAAA requirement) o 18 - 64, 65 - 84, ≥ 85 (EMA requirement) • Race: o White, Non-White o Black/African American, Non-Black/African American For the statistical modelling, only White vs Non-White is considered. • Sex at birth: o Female o Male • Country (not used for statistical modelling) o Argentina o Australia o Canada o France o Germany o Italy o Korea, Republic of o Mexico o Russian Federation

Category	Covariates and / or Subgroups
	○ South Africa ○ Spain ○ Sweden ○ United States • Baseline CD4+ cell count (cells/mm^3): ○ <350 ○ 350 - < 500 ○ ≥ 500 • Baseline HIV-1 RNA (c/mL): ○ <50 ○ ≥ 50 • Derived Baseline Centers for Disease Control and Prevention (CDC) category: ○ Stage I ○ Stage II ○ Stage III • Prior Exposure to CAB+RPV: ○ 0 weeks ○ ≥ 1 weeks This subgroup will be used in efficacy analysis, in addition to the redrived randomization strata (prior exposure to CAB+RPV: 0, 1-24, and >24 weeks). It will also be used in health outcomes analysis. In other types of analysis, only the rederived randomization strata will be used. • Baseline BMI (kg/m^2) ○ <30 ○ ≥30 • Baseline Third Agent Class: ○ None (for subjects with prior exposure to CAB+RPV in ATLAS, i.e. subjects transitioned from ATLAS) ○ NNRTI ○ INI ○ PI
EMA Subgroup Category 3:	
Additional subgroup/covariates for PK/PD efficacy analysis	PK/PD efficacy analysis will be performed for participants without prior exposure to CAB + RPV. • Week 8 CAB/RPV Trough PK concentration (i.e. pre-dose PK concentration at nominal visit of Week 8) The above covariate will be dichotomized into two subgroup factors as follows: ○ ≤ first Quartile vs > first quartile, ○ ≤ Median vs > Median The concentration will also be treated as continuous variable in logistic regression modelling analysis (i.e. the concentration data will be log_2 transformed in this analysis so that, for assessing the effect,

Category	Covariates and / or Subgroups
	one unit increase of the point estimate of log2 PK concentration is equivalent to 'doubling the concentration' in the original value). • Length of First CAB/RPV Injection Needle (<2, ≥2 inches)
Additional subgroup/covariates for PK/PD safety analysis	Last CAB/RPV trough PK concentration For the plot of Maximum Change from Baseline(CFB) in ALT/Total Bilirubin versus Last Trough CAB/RPV PK Concentrations, Last CAB/RPV Trough PK Concentration is the most recent trough PK concentration prior or equal to the date of the lab assessment with maximum CFB during the maintenance phase. For the Plot of Maximum Toxicity Grades of Most Frequently Reported Study Drug ISR adverse events (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 the most frequently reported Study Drug ISR AE with maximum toxicity grade, during the maintenance phase. If a participant has no Study Drug ISR AE most commonly reported, then the last trough value during the maintenance phase will be used for the plot.
Additional subgroup for common drug-related study drug injection site reaction (ISR) with maximum toxicity grade	For each preferred term of the common drug-related study drug ISR with maximum toxicity grade (pain, induration, nodules and any other study drug ISR with >=5% subjects in either treatment arm) during the maintenance phase: • 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: ≤1.5, >1.5 to <2, ≥2 inches • 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: ≤1.5, >1.5 to <2, ≥2 inches Note: If there is no ISR of interest reported during maintenance phase for a subject, the needle length of last injection during maintenance phase will be used in the summary.

5.5. Multiple Comparisons and Multiplicity

5.5.1. Primary Comparison of Interest

The primary analysis will be based on the ITT-E population. The primary comparison will be made at a one-sided 2.5% level of significance. Treatment with Q8W will be declared non-inferior to Q4W if the upper end of a two-sided 95% confidence interval for the difference between the two groups (Q8W – Q4W) in the proportion of participants with HIV-1 RNA ≥50 c/mL at Week 48 (defined by the US FDA snapshot algorithm) lies below 4%.

The primary comparison of interest is the comparison between Q8W (CAB LA + RPV LA Q8W) and Q4W (CAB LA + RPV LA Q4W) for the primary endpoint in the ITT-E population. This analysis will be adjusted for by the re-derived randomization strata based on eCRF data.

5.5.2. Other Comparisons of Interest

If the primary comparison of interest (Section 5.5.1) using the ITT-E population demonstrates non-inferiority of Q8W compared to Q4W then the following key secondary comparisons will be tested:

- Treatment with Q8W will be declared non-inferior to Q4W with respect to the proportion of participants with HIV-1 RNA < 50 c/mL at Week 48 (defined by the US FDA snapshot algorithm) if the lower end of a two-sided 95% confidence interval for the difference between in rates (Q8W – Q4W) lies above -10% using the ITT-E population
- Superiority of Q8W compared to Q4Wwith respect to change from baseline HIVTSQs total score at Week 48 using the ITT-E population and a two-sided 5% level of significance. Refer to Section 12.5.1 for details.

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. The primary endpoint treatment comparison at Week 48 will also be performed using the PP population and the results will be compared for consistency with the results from the ITT-E population.

In addition to the primary and the key secondary comparisons, the comparisons between two treatment arms for ACCEPT (general acceptance score), PIN (Domain scores ([redacted], and [redacted]) and Individual Items Scores ([redacted])), HAT-QoL (Life satisfaction, HIV medications, disclosure worries) and HIVTSQc (Treatment Satisfaction score) 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
15.3	Appendix 3: Assessment Windows
15.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events

Section	Component
15.5	Appendix 5: Data Display Standards & Handling Conventions
15.6	Appendix 6: Derived and Transformed Data
15.7	Appendix 7: Reporting Standards for Missing Data
15.8	Appendix 8: Values of Potential Clinical Importance
15.9	Appendix 9: Snapshot Algorithm Details
15.10	Appendix 10: Variables Defined for Time to Event Analysis
15.11	Appendix 11: Identification of Adverse Events of Special Interest
15.12	Appendix 12: IDMC

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 oral study treatment accountability will be based on GSK Core Data Standards.

Table 1 provides an overview of the planned study population analyses, with details of the planned displays are presented in Appendix 14: List of Data Displays.

Table 1 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated	
	Table	Listing
Randomization		
Randomization [1]		Y[2]
Subject Disposition		
Study Populations [3]	Y	
Study Recruitment [3]	Y	
Reasons for Screening Failures [3]	Y	Y
Rescreened Subjects [3]		Y
Age Ranges	Y	
Subject Disposition	Y[4][5]	
Reasons for Withdrawal	Y[4][5]	Y
IP Discontinuation	Y	Y
Important Protocol Deviations	Y	Y

Display Type	Data Displays Generated	
	Table	Listing
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 Entry	Y	
Baseline CDC Classification of HIV infection (2014)	Y	
Baseline Cardiovascular Risk Assessments	Y	
Distribution of CD4+ Cell Counts at Screening and Baseline	Y	
Prior Exposure to CAB+RPV	Y	
HIV-1 Risk Factors	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 ART Medications	Y	Y
Concomitant ART Medications during Maintenance Phase		Y
ART Medications Received during LTFU Phase		Y
Lipid Modifying Agents (Baseline and during Maintenance Phase)	Y	
Substance use at Entry	Y	
Medical History of Seizure		Y
Other		
Oral Study Treatment Accountability [11]		Y

NOTES:

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

1. Base on Randomized population.
2. One listing of participants randomized but not treated, and one listing of randomized and actual strata and treatment assignment.
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.
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).

6.2. Prior and Concomitant Medications

Non-ART and/or ART Medications will be classified by categories shown in Table 2. The same medication may be classified by more than one categories. For example, if the Non-ART medication was started after the maintenance treatment start date and was stopped at nominal Week 104 visit while subject was still receiving study treatment, this medication would be considered both 'concomitant during maintenance' and 'concomitant during extension'.

Table 2 Derived Data for Non-ART Medications/ART Medications

	Definition
Prior	ART Medication Taken ≤ Maintenance Treatment Start Date Non-ART Medication Taken < Maintenance Treatment Start Date
Concomitant during Maintenance	**For subjects continuing into Extension Phase:** Maintenance Treatment Start Date ≤ Non-ART Medication Taken < Date of Nominal Week 100 Visit Maintenance Treatment Start Date < ART Medication Taken ≤ Date of Nominal Week 100 Visit **For subjects not continuing into Extension Phase[a]:** Maintenance Treatment Start Date ≤ Non-ART Medication Taken < LTFU ART Start Date Maintenance Treatment Start Date < ART Medication Taken < LTFU ART Start Date
Concomitant during Extension	**For subjects continuing into Extension Phase[a]:** Date of Nominal Week 100 Visit ≤ Non-ART Medication Taken < LTFU ART Start Date Date of Nominal Week 100 Visit < ART Medication Taken < LTFU ART Start Date
Received during Long-term Follow-up	**For subjects Who received at least one CAB and/or RPV injection and have started LTFU ART:** Non-ART/ART Medication Taken ≥ LTFU ART Start Date

NOTES:

- Please refer to Appendix 7: Reporting Standards for Missing Data for handling of missing and partial dates for medications. Use the rules in this table if medication date is completely missing.
- [a] If subjects have missing LFTU ART start date, only the lower bound will be considered in the derivation.

7. EFFICACY ANALYSES

7.1. Primary Efficacy Analyses

7.1.1. Endpoint / Variables

Proportion of participants with plasma HIV-1 RNA ≥50 c/mL as per Food and Drug Administration (FDA) Snapshot algorithm at Week 48 (Intent-to-Treat Exposed [ITT-E] population); see Section 15.9 for additional details.

7.1.2. Summary Measure

Difference in the proportion of participants with HIV-1 RNA ≥50 c/mL at Week 48 (defined by the US FDA snapshot algorithm) between each treatment group (Q8W – Q4W).

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-1 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 on-treatment HIV-1 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-1 RNA ≥ 50 c/mL.

7.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 14: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 7.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

7.1.5.1. Statistical Methodology Specification

Endpoint
• Proportion of Participants with plasma HIV-1 RNA ≥ 50 c/mL at Week 48 using the Snapshot algorithm for the ITT-E population. Subjects with 'HIV-1 RNA ≥ 50 c/mL' per Snapshot algorithm include those 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-1 RNA <50 c/mL' or 'HIV-1 RNA ≥ 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 10). In addition, subjects who discontinue for reasons not related to adverse event with on-treatment HIV-1 RNA result at the time of discontinuation ≥ 50 c/mL or who change study treatment not permitted per protocol during maintenance phase before the analysis visit are classified as 'HIV-1 RNA ≥ 50 c/mL'.
- Full details of the Snapshot algorithm are provided in Section 15.9.

Model Specification

- The primary efficacy endpoint will be analysed using a stratified analysis with Cochran-Mantel-Haenszel (CMH) weights, adjusting for the rederived randomization strata corresponding to prior exposure to CAB+RPV (0 weeks, 1-24 weeks, >24 weeks)
- 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 stratum as follows:
    - If n_k is the number of Q8W treated participants, m_k is the number of Q4W arm treated participants, and $N_k = n_k + m_k$ is the total number of participants in the kth 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_{Q8W}-f_{Q4W}, for the *kth* stratum.

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

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

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 ≥ 50 c/mL at Week 48 per FDA Snapshot for Q8W and Q4W, respectively, for the *kth* stratum.

Model Results Presentation

- Adjusted CMH estimate of the difference in the proportion of subjects with Plasma HIV-1 ≥ 50 c/mL between each treatment group (Q8W – Q4W) and corresponding 95% confidence interval.
- Non-inferiority will be concluded if the upper bound of the two-sided 95% confidence interval for the CMH adjusted treatment difference (Q8W – Q4W) is less than 4%.
- If this analysis shows non-inferiority, then a superiority hypothesis will be tested at the two-sided 5% level of significance. Superiority favoring Q8W will be declared if the upper bound 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.

Subgroup Analyses

1. Treatment Heterogeneity across rederived randomization strata [prior exposure to CAB+RPV (0 weeks, 1-24 weeks, >24 weeks)]:
   - 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 f_{Q8W} or f_{Q4W} 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 endpoint. Tests of homogeneity will be assessed at the one-sided 10% level of significance.

2. Stratum-specific analyses for two groups of participants: (Group 1) those currently receiving Standard of Care antiretroviral therapy at Baseline (i.e. no prior exposure to CAB+RPV), (Group 2) those receiving Q4W CAB LA + RPV LA therapy in the ongoing ATLAS study (i.e. have prior exposure to CAB+RPV). For each stratum (Group 1 and Group 2), the following will be presented:
   - Proportion of subjects with plasma HIV-1 RNA ≥ 50 c/mL at Week 48 by treatment group.
   - Unadjusted difference in proportions between treatment groups and corresponding two-sided 95% CI.
   - Summary of study outcomes (i.e. HIV-1 RNA < 50 c/mL, HIV-1 RNA ≥50 c/mL and reason for no data in the window)

For Group 2, a stratum-adjusted analysis will also be provided, with adjustment for prior CAB+RPV

exposure (1 to 24 weeks vs. >24 weeks) using Cochran-Mantel Haenszel (CMH) weights, as described in the model specification above for the overall primary analysis.

3. Exploration of Subgroups
   - An analysis for subgroups listed in Section 5.4.2 will be performed. This will show the proportion of subjects with plasma HIV-1 RNA ≥50 c/mL at the time of analysis (Week 48) based on the Snapshot algorithm and will be presented by treatment group.
   - Unadjusted difference in proportions between treatment groups and corresponding two-sided 95% CI will also be presented by subgroups. The confidence interval will be calculated using an unconditional exact method [Chan et al, 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. HIV-1 RNA < 50 c/mL, HIV-1 RNA ≥50 c/mL 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. Endpoints

The key secondary efficacy endpoint is the 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).

Other secondary efficacy endpoints for the study are listed below:

- Proportion of participants with plasma HIV-1 RNA < 50 c/mL at Week 24 and Week 96 using the FDA Snapshot algorithm (ITT-E population)
- Proportion of participants with protocol-defined confirmed virologic failure (CVF) through Week 24, Week 48 and Week 96
- Proportion of participants with HIV-1 RNA ≥50 c/mL as per FDA Snapshot algorithm at Week 24 and Week 96
- Absolute values and changes from Baseline in viral load and CD4+ cell counts over time including Week 48 and Week 96

7.2.2. Summary Measure

Difference in the proportion of participants with HIV-1 RNA < 50 c/mL at Week 48 and Week 96 (defined by the US FDA snapshot algorithm) between each treatment group (Q8W – Q4W).

Difference in the proportion of participants with HIV-1 RNA ≥ 50 c/mL at Week 24 and Week 96 (defined by the US FDA snapshot algorithm) between each treatment group (Q8W – Q4W).

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

As defined by the snapshot algorithm, 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.

Participants without on-treatment HIV-1 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-1 RNA ≥ 50 c/mL.

7.2.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 14: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 7.2.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

7.2.5.1. Statistical Methodology Specification

Key Secondary Statistical Analysis
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 Section 7.1.5.1 and Section 15.9
Model Specification
• As specified in Section 7.1.5.1 but with 'HIV-1 RNA <50 c/mL' replacing HIV-1 ≥ 50 c/mL
Model Results Presentation
• Adjusted CMH estimate of the difference in the proportion of participants with HIV-1 RNA < 50

Key Secondary Statistical Analysis
c/mL at Week 48 between each treatment group (Q8W – Q4W) and corresponding 95% confidence interval. • Non-inferiority will be concluded if the lower bound of the two-sided 95% confidence interval for the CMH adjusted treatment difference (Q8W – Q4W) is greater than -10%.
Subgroup Analyses
• As specified in Section 7.1.5.1 but with HIV-1 RNA < 50 c/mL replacing 'HIV-1 RNA ≥ 50 c/mL.
Sensitivity and Supportive Analyses
1. Per-protocol population analysis: • To assess the impact of important protocol deviations, statistical analysis will be repeated using the Per-protocol population and compared for consistency with the results from the primary ITT-E population analysis.

7.3. Exploratory Efficacy Analyses

Table 3 provides an overview of the planned exploratory efficacy analyses. Details of the planned displays are provided in Appendix 14: List of Data Displays and will be based on GSK data standards and statistical principles. The exploratory efficacy analyses will be based on the Intent-to-Treat Exposed population, unless otherwise specified.

Table 3 Overview of Exploratory Efficacy Analyses

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Proportion of participants without efficacy-related discontinuation (ERDF) or treatment-related discontinuation (TRDF) failure at Week 24/Week 48/Week 96														
Kaplan-Meier estimate				Y										
Proportion of participants with plasma HIV-1 RNA ≥50 c/mL over time (Maintenance Phase) - Snapshot														
by visit				Y	Y[1]									
By visit and subgroup				Y	Y[2]									
Proportion of participants with plasma HIV-1 RNA <50 c/mL over time (Maintenance Phase) - Snapshot														
by visit				Y	Y[3]									
By visit and subgroup				Y	Y[2]									
Proportion of participants with plasma HIV-1 RNA ≥200 c/mL over time (Maintenance Phase) - Snapshot														
by visit				Y[4]	Y[5]									
Proportion of participants with plasma HIV-1 RNA <200 c/mL over time (Maintenance Phase) - Snapshot														
by visit				Y[4]	Y[5]									
Proportion of participants with plasma HIV-1 RNA ≥50 c/mL at Week 48/Week 96 by delay in IP injection - Snapshot														
by delay in IP injection [6]				Y										
Proportion of participants with plasma HIV-1 RNA <2 c/mL over time (Maintenance Phase)														
by visit				Y										
Plasma HIV-1 RNA over time														
by visit				Y[7]		Y[8]	Y[9]							Y[9]
Target Detected vs Target Not Detected by visit [10]				Y			Y[11]							
Confirmed Virologic Failure (CVF)														
CVF overall				Y										
CVF by visit				Y			Y							

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Plasma HIV-1 RNA at time of suspected and confirmed virologic failure				Y										
CD4+ & CD8+ Cell Counts Over Time														
CD4+ observed [12]				Y							Y			
CD8+ observed [12]				Y							Y			
CD4+/CD8+ ratio observed [12]				Y										
HIV-1 Conditions and Disease Progression														
HIV Conditions including/excluding Recurrences as recorded in eCRF				Y			Y							
HIV Disease Progressions [13]				Y										

NOTES:

- T = Table, F = Figures, L = Listings, Y = Yes display generated
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TF related to any summaries (i.e. descriptive statistics) of data.
- Individual = Represents FL related to any displays of individual participant's data.

1. Line plots, with 95% confidence intervals (CIs), for the proportion of participants with HIV-1 RNA ≥50 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%; otherwise, they are derived using the normal approximation.
2. Plot of the unadjusted treatment difference and its 95% confidence intervals (Snapshot algorithm) overall and by subgroup at Week 48/Week 96.
3. Line plots, with 95% confidence intervals, for the proportion of participants with HIV-1 RNA<50 c/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.
4. Study outcomes (i.e., HIV-1 RNA <200 c/mL, HIV-1 RNA ≥200 c/mL, or reason for no data in the window) based on the snapshot algorithm at Week 48 will also be produced.
5. Line plots, with 95% confidence intervals, for the proportion of participants with HIV-1 RNA <200 c/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.
6. Delay in IP injection (days) is defined in Section 15.6.3.
7. Using log10 transformed values.
8. 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.
9. For CVF participants, participants with viral load ≥ 50 c/mL during the Maintenance Phase, and participants with viral load ≥ 50 c/mL during the Maintenance oral lead-in period.
10. See Section 15.6.3 for definition of "Target Detected" and "Target Not Detected", and for the specification of corresponding summary table.
11. Target Detected" and "Target Not Detected" are included in the listing for plasma HIV-1 RNA by visit.
12. Using available data without imputation for missing values.
13. See Section 15.6.3 for HIV disease progressions.

8. SAFETY ANALYSES

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

8.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Section 15.14: List of Data Displays.

8.1.1. Analyses for Injection Site Reaction Adverse Events from Study Drug Injection

Injection Site Reaction (ISR) adverse events of interest are those from study drug injections. For the summary of study drug ISR adverse events by visit and maximum severity (overall and by common ISRs): ISRs will be assigned based on onset date to the most recent planned IM injection visit prior or equal to the AE onset date.

Maximum grade at each visit will be derived as the maximum grade among ISRs assigned to the particular visit, with consideration for whether the summary applies to a particular preferred term (vs. across preferred terms), drug-related associated to CAB and/or RPV, or stratification by subgroup (such as needle length, refer to Section 5.4.2).

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

Common study drug ISR adverse events are defined by MedDRA preferred terms including injection site pain, injection site induration, injection site nodules and preferred terms of any other ISR with ≥5% participants in either treatment arm, coming from study drug injections. The same set of common terms will be applied to ‘overall’ (CAB and/or RPV), CAB alone, RPV alone.

Study drug ISRs will be attributed to the needle length (≤1.5, >1.5 to <2, ≥ 2 inches) 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 for 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.

8.2. Adverse Events of Special Interest Analyses

Adverse events of special interest (AESI) are determined for CAB and/or RPV based on pre-clinical and clinical experience, along with information for the Integrase Inhibitor class of HIV medications and RPV safety profile. Table 4 shows the currently identified AESI, drug(s) of Interest and the reasons for inclusion. 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 AESIs may change at the time of reporting.

A summary by system organ class and preferred term will be provided for each of AESI. The characteristics of event occurrences during the maintenance phase will be summarized for common AESI which have at least 20 participants in either treatment arm. For Depression, anxiety and suicidal ideation/behaviour AESI, a summary by system organ class, maximum DAVIDS toxicity grade and prior history of suicidal ideation will be provided. The details of the planned grouping and planned displays are provided in Section 15.11 and Appendix 14: List of Data Displays.

Table 4 Adverse Events of Special Interest

Adverse Events of Special Interest	Drug(s) of Interest	Reason for Inclusion
Hepatic Safety Profile: Assessment of Risk of hepatoxicity	CAB+RPV	Clinical, Class, Regulatory Interest, More prevalent in HIV population
Hypersensitivity Reactions (HSR)	CAB	Class, Regulatory Interest, Occurs in HIV population
Rash	RPV	Class, Regulatory Interest, Occurs in HIV population
Prolongation of the Corrected QT Interval of the ECG in Supratherapeutic Doses	RPV	Non-clinical, Clinical, Regulatory Interest
Suicidal Ideation/Behaviour	CAB+RPV	Clinical, Class, Regulatory Interest, More prevalent in HIV population
Depression	CAB+RPV	Clinical, Class, Regulatory Interest, More prevalent in HIV population
Bipolar Disorder	CAB+RPV	Clinical, Class, Regulatory Interest, More prevalent in HIV population
Psychosis	CAB+RPV	Clinical, Class, Regulatory Interest, More prevalent in HIV population
Mood Disorders	CAB+RPV	Clinical, Class, Regulatory Interest
Anxiety	CAB+RPV	Clinical, Class, Regulatory Interest
Sleep Disorders	CAB+RPV	Clinical, Class, Regulatory Interest, More prevalent in HIV population
Injection Site Reactions (ISR) from Study Drug Injections [1]	CAB+RPV	Clinical

Adverse Events of Special Interest	Drug(s) of Interest	Reason for Inclusion
Seizures and Seizure-like Events	CAB	Clinical, Regulatory Interest
Weight Gain	CAB	Clinical, Class
Rhabdomyolysis	CAB	Clinical, Class
Pancreatitis	CAB	Clinical, Therapeutic Area, More prevalent in HIV population
Impact on Creatinine	CAB+RPV	Regulatory Interest, Therapeutic Area, More prevalent in HIV population
Safety in Pregnancy	CAB	Regulatory Interest, Class
NOTE: [1] A separate analysis will be performed for ISRs from study drug injections as described in Section 8.1.1.		

8.3. Clinical Laboratory Analyses

Laboratory evaluations including the analysis of results of Chemistry laboratory tests, Haematology laboratory tests, Urinalysis, and liver function tests will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 14: 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 14: List of Data Displays.

ECG values of potential clinical importance are defined as a QTc of > 500 msec or increase from baseline in QTc ≥ 60 msec.

9. PHARMACOKINETIC ANALYSES

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

9.1. Endpoint / Variables

9.1.1. Drug Concentration Measures

Refer to Appendix 5 Data Display Standards & Handling Conventions (Section 15.5.3 Reporting Standards for Pharmacokinetic)

9.2. Overview of Planned Analyses

Table 5 provides an overview of the planned analyses with full details being presented in Appendix 14: List of Data Displays. All PK displays will be based on the PK Population, unless otherwise specified.

Table 5 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						

NOTES:

- T = Table, F = Figure, L = Listings, Y = Display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TF 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.
- Unless otherwise specified, all displays for evaluable concentrations except for individual displays will be presented by both overall and the rederived randomization strata.

1. For both 'all' concentration and the 'evaluable' concentration. The evaluable concentration is derived from samples collected within pre-specified Time window (Section 15.6.5)
2. For both 'untransformed' and 'log–transformed' statistics.
3. The plots will be produced for the untransformed scale (i.e., a linear plot) and the log transformed scale (i.e., log-linear plot), separately.
4. Separate plots will be produced for Mean (SD) and Median concentration.
5. Standard summary statistics for concentration data will be calculated (i.e., mean, standard deviation, coefficient of variation, median, minimum and maximum). For Logarithmically transformed data, the summary statistics (i.e. geometric mean, between subject coefficient of variation, 95% confidence interval for the geometric mean and standard deviation) will also be calculated.

9.3. Statistical Analyses / Methods

Planned PK statistical analysis
Steady State Concentration
Endpoints
• log_e-transformation of the Trough/Pre-dose evaluable plasma concentrations (CAB/RPV) on Week 16-48 (i.e. Weeks 16, 24, 32, 40 and 48) for participants receiving Q8W study treatment
Covariates
• Study Week
Data Handling
• All data remains as is (observed).
Model Specification
• A mixed effects ANOVA model will be fitted for each rederived randomization stratum [prior exposure to CAB+RPV (0 weeks, 1-24 weeks, >24 weeks)] with Study 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 week effect on the loge-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, 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 week effect on the log_e-scale, its standard error and 90% interval will be presented for each rederived randomization stratum.

10. POPULATION PHARMACOKINETIC ANALYSES

The Population PK analyses will be described under a separate Population-PK Reporting and Analysis Plans for CAB LA and RPV LA

11. PHARMACOKINETIC / PHARMACODYNAMIC ANALYSES

The primary goal of this analysis is to characterize the pharmacokinetic / pharmacodynamic relationship of CAB/RPV administered in participants with HIV-1-infection who are virologically suppressed. The influence of subject demographics and

baseline characteristics and additional subgroups/covariates in this population will be investigated.

11.1. Overview of Planned Analyses

Table 6 provides an overview of the planned analyses with full details being presented in Appendix 14: List of Data Displays. All PK displays will be based on the PK Population, unless otherwise specified.

Table 6 Overview of Planned Pharmacokinetic / Pharmacodynamic Analyses

	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
CAB/RPV Week 8 concentrations by snapshot 'HIV-1 RNA ≥50 c/mL' (Yes vs. No) for participants without prior exposure to CAB+RPV				Y	Y		
Analysis of snapshot 'HIV-1 RNA ≥50 c/mL' at Week 48 by Week 8 trough concentration, and subgroup [1] – univariable analysis /multivariable analysis for participants without prior exposure to CAB+RPV	Y						
Individual CAB/RPV concentration-time profiles for participants with snapshot 'HIV-1 RNA ≥50 c/mL' at Week 48 or 96					Y		
Maximum change from baseline in ALT/Total Bilirubin versus last trough CAB/RPV concentrations [2]					Y		
Maximum toxicity grades of most frequently reported study drug ISR AEs [3] versus last trough CAB/RPV PK concentrations [2]					Y		

NOTES:

- T = Table, F = Figure, L = Listings, Y = Display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TF 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. Refer to Section 11.2.
2. Display by rederived randomization strata, i.e. prior exposure to CAB+RPV (0, 1-24, >24 weeks) derived based on eCRF.
3. Most frequently reported study drug ISR AEs are those top 5 in incidence in either treatment arm (i.e. Q8W or Q4W arm).

11.2. Statistical Analyses / Methods

PK/PD Efficacy Analysis for Participants without Prior Exposure to CAB+RPV
Endpoints
• Snapshot 'HIV-1 RNA≥50 c/mL' at Week 48 (or W96)

Covariates
• Treatment, demographic and baseline characteristics except for country and Prior Exposure to CAB+RPV (0, ≥1 weeks), and additional subgroup/covariates for PK/PD efficacy analysis - 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 c/mL') at Week 48 and the covariates/subgroups. This logistic regression analysis will be performed for each covariate or subgroup, separately (univariable analysis), and will also be performed with one multivariable analysis using Backward stepwise selection approach to identify the covariates/subgroups potentially affecting virologic response.
Model Checking & Diagnostics
• For the multivariable analysis, a logistic regression model that best predicts the dependent variable (i.e. snapshot 'HIV-1 RNA≥50 c/mL') from the independent variables (i.e. covariates/factors with P <0.15 from univariable analysis) will be determined using the backward stepwise selecting approach. 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%. • 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.

12. HEALTH OUTCOMES ANALYSES

12.1. Endpoint / Variables

- Preference between injections of LA HIV treatment and daily oral HIV treatment at Week 48
- Preference between LA injection every 8 weeks and LA injection every 4 weeks at Week 48 (Q8W arm only)
- Change from baseline in total "treatment satisfaction" score, and individual item scores of the HIV Treatment Satisfaction Status Questionnaire (HIVTSQs) at Weeks 24 and 48
- Change from baseline in life satisfaction, HIV medication, and disclosure worries using HIV/AIDS Targeted Quality of Life (HAT-QoL) at Weeks 24 and 48

- Change in treatment satisfaction over time using the HIV Treatment Satisfaction Change (HIVTSQc) questionnaire at Week 48
- Change from Week 8 in Dimension Scores 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 Perception of Injection (PIN) questionnaire at Weeks 24 and 48
- Change from baseline in treatment acceptance using ACCEPT at Weeks 24 and 48
- Reasons for continuation of receiving injectable HIV treatment at Baseline (Day 1) visit. This is an exploratory endpoint.
- Reasons for switching to injectable HIV treatment at Baseline (Day 1) visit. This is an exploratory endpoint.

12.2. Summary Measure

Mean treatment difference (Q8W – Q4W) at visits of interest, except for Preference between LA injection every 8 weeks and LA injection every 4 weeks at Week 48.

12.3. Population of Interest

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

Analysis of Reason for continuation will be based on a subset of the Intent-to-Treat Exposed population who were randomized to Q4W arm in ATLAS (i.e. ATLAS Q4W population).

Analysis of Reason for switch will be based on a subset of Intent-to-Treat Exposed population who either were randomized to SOC arm in ATLAS or did not participate in ATLAS study (i.e. SOC population).

12.4. Strategy for Intercurrent (Post-Randomization) Events

If a participant discontinues treatment prior to the timepoint of interest such that there is no evaluable assessment for the timepoint of interest, the data will be computed or imputed (see Section 15.6.6).

12.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 14: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 12.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

12.5.1. Statistical Methodology Specification

Statistical Analyses
Endpoints

• Change from Baseline in
  ○ HIVTSQs total treatment satisfaction score at Weeks 24 and 48
  ○ ACCEPT general acceptance score at Weeks 24 and 48
  ○ HAT-QoL (Life satisfaction, HIV medications, disclosure worries) at Weeks 24 and 48
• Change from Week 8 in PIN Domain Scores (CCI [redacted], and CCI [redacted]) and Individual Items Scores (CCI [redacted], CCI [redacted]) at Weeks 24 and 48

Model Specification

• The analysis for HIVTSQs, ACCEPT and HAT-QoL will be performed for subjects with and without prior exposure to CAB+RPV separately.
  ○ For subjects without prior exposure to CAB+RPV, an analysis of covariance (ANCOVA) model will be used at each visit during the maintenance phase with covariates: treatment, age (<50, ≥ 50 years old), sex at birth, race (i.e. white, non-white) and baseline score value for other endpoints (as a continuous variable).
  ○ For subjects with prior exposure to CAB+RPV, an analysis of covariance (ANCOVA) model will be used at each visit during the maintenance phase with covariates: treatment, age (<50, ≥ 50 years old), prior exposure to CAB+RPV (i.e. 1 to 24 weeks, >24 weeks), sex at birth, race (i.e. white, non-white) and baseline score value (as a continuous variable).
• For PIN, an analysis of covariance (ANCOVA) model will be used at each visit during the maintenance phase with covariates: treatment, age (<50, ≥ 50 years old), prior exposure to CAB+RPV (i.e. 0 weeks, 1 to 24 weeks, >24 weeks), sex at birth, race (i.e. white, non-white), and Week 8 score value (as a continuous variable).
• Adjusted point estimates will be derived as LSMEANS using the observed margins (OM) option within PROC MIXED in SAS.
• The superiority testing of Q8W compared to Q4W with respect to change from baseline in HIVTSQs total score at Week 48 will be performed using the fixed sequence procedure to control for the type I error rate at the nominal level of 5%. If the superiority testing within subjects without prior exposure to CAB+RPV demonstrates Q8W is superior to Q4W in change from baseline in HIVTSQs total score at Week 48 at two-sided 5% level of significance, the superiority testing at the same level of significance (i.e. two-sided 5%) within subjects with prior exposure to CAB+RPV will be followed. No adjustment for multiplicity will be applied for other tests as they will be considered supportive.
• 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

Statistical Analyses
• Adjusted treatment difference (Q8W – Q4W), its 95% CI and the associated p-value. The interaction between treatment and the baseline score will be included in a footnote. • Plots of adjusted mean change from baseline (95% CI) for each treatment group, and the adjusted mean difference (95%CI) between the two treatment arms from the model will be generated across visit.

Statistical Analyses
HIVTSQc
• Total 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), prior exposure to CAB+RPV (i.e. 0 weeks, 1 to 24 weeks, >24 weeks), sex at birth and race (i.e. white, non-white). • Adjusted point estimates will be derived as LSMEANS using the observed margins (OM) option within PROC MIXED in SAS. • 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. • 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 (Q8W – Q4W).

Statistical Analyses
PIN
• Change from Week 8 in the PIN acceptance score at Week 24 and Week 48
Statistical Test
• The Wilcoxon Signed-Rank Test will be used to evaluate whether the change from Week 8 to Week 24 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 8 to Week 24 and for the change from Week 8 to Week 48.
Dataset
• LOCF dataset will be used
Results Presentation
• Summary statistics at each timepoint (Week 8, Week 24 and W48) and p-value for each comparison between scores at Week 24/48 with scores at Week 8.

13. VIROLOGY

The virology analyses will mainly use genotype and phenotype data based on plasma sample for CVF population, unless otherwise specified. Additional analyses for HIV-1 resistance may be carried out on peripheral blood mononuclear (PBMC) samples collected at Day 1, Week 48, 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.

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

Table 7 Overview of Planned Virology Analyses

Endpoint	Absolute			
	Summary		Individual	
	T	F	F	L
Genotypic resistance at time of CVF[1]				
Prevalence of Resistance Mutations	Y [2]			Y
Prevalence of Genotypic Susceptibility	Y			
Phenotypic resistance at time of CVF[1]				
Prevalence of Phenotype	Y [3]			Y
Fold Change to CAB and RPV	Y			Y[4]
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]
Net Assessment	Y			

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual 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, 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 may be used for exploratory analyses.
2. No. and percentage of participants with IN resistance mutations or major mutations in the classes of NNRTI, NRTI, PI, respectively, as defined in Section 15.6.7.
3. Separate outputs by phenotypic susceptibility and by number of drugs to which participants are phenotypic resistant or partial sensitive or sensitive.
4. Fold change to CAB and RPV will be included in the listing for viral load, genotypic and phenotypic data for participants with genotype and/or phenotype data for CVF and non-CVF participants.

14. REFERENCES

Chan, I. S. F. and Zhang, Z. (1999), "Test-Based Exact Confidence Intervals for the Difference of Two Binomial Proportions," Biometrics, 55, 1202–1209.

Chevat C, Viala-Danten M, Dias-Barbosa C, Nguyen VH. Development and psychometric validation of a self-administered questionnaire assessing the acceptance of influenza vaccination: the Vaccinees' Perception of Injection questionnaire. Health Qual Life Outcomes. 2008 mar 4; 7:21

D'Agostino RB, Vasan RS, Pencina MJ, et al. General Cardiovascular Risk Profile for Use in Primary Care (The Framingham Heart Study). Circulation 2008; 117: 743-753.

EMA/CHMP/539146/2013, Guideline on the investigation of subgroups in 4 confirmatory clinical trials, 23 January 2014

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

Gilet H, Arnould B. Acceptance by the patients of their treatment (ACCEPT) Questionnaire, 2014.

Grundy S.M., et al. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA. 2001; 285 (19): 2486-2497.

HIVTSQ user guidelines, Health Psychology Research Unit, Royal Holloway, University of London, 2016

Holmes WC, HIV/AIDS-Targeted Quality of Life Instrument 1999.

Kalbfleisch J.D., Prentice R.L. *The Statistical Analysis of Failure Time Data.* 1st ed. New York: John Wiley & Sons; 1980.

Levey AI, Christopher HS, Hocine T, John HE, Harold IF, Tom G, et al. Esitmating Glomerular Filtration Rate from Serum Creatinine and Cystatin C. N Engl J Med 2012, 367: 20-29.

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

Nilsson ME, Suryawanshi S, Gassmann-Mayer C et al, Columbia–Suicide Severity Rating Scale, Scoring and Data Analysis Guide, 2013.

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

Wensing AM et al. Update of the Drug Resistance Mutations in HIV-1 Volume 24 Issue 4 December 2016/January 2017

15. APPENDICES

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

15.1.1. 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 important 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 any 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 maintenance phase non-compliance (including IM dosing errors) with investigational product up to an analysis timepoint of interest, meeting one of the following 3 conditions. For Week 48 analysis, the analysis timepoint of interest is the date of last on-treatment viral load up to Study Day 378 during maintenance phase, where Study Day 378 is the upper bound of snapshot window for Week 48 visit. For Week 96 analysis, the analysis timepoint of interest is the date of last on-treatment viral load up to Study Day 714 during the maintenance phase, where Study Day 714 is the upper bound of snapshot window for Week 96 visit. 1. Week 48 analysis only: • Two or more injection intervals affected by over dosage deviations, for example o Extra injection or excessive volume administered. o For Q8W participants requiring oral lead-in: length of time between Week 4B injection and Week 8 injection less than 3 weeks, or between injections post Week 8 less than 7 weeks, excluding split doses. o For Q8W participants not requiring oral lead-in: length of time between injections less than 7 weeks, excluding split doses. o For Q4W participants: length of time between injections less than 3 weeks, excluding split doses. 2. Week 96 analysis only: • For participants who permanently discontinued study treatment on/before the

Number	Exclusion Description
	analysis timepoint of interest for Week 48 analysis (i.e. the date of last on-treatment viral load up to Study Day 378): two or more injection intervals affected by over dosage deviations. • For participants who received injections beyond the analysis timepoint of interest for Week 48 analysis (i.e. the date of last on-treatment viral load up to Study Day 378): three or more injection intervals affected by over dosage deviations. 3. ≥ 10% of total time on-treatment with under dosing deviations. The percentage of total time on-treatment with under dosing deviations will be calculated by (the total number of non-compliant dosing days / the total number of intended exposure days) * 100%. Number of Intended Exposure Days = Date of Last Viral Load – Start Date of Study Treatment + 1, where the last viral load refers to the last on-treatment viral load up to Study Day 378 during maintenance phase for Week 48 analysis, and the last on-treatment viral load up to Study Day 714 during maintenance phase for Week 96 analysis. The total number of non-compliant dosing days up to the analysis timepoint visit (or date of IP discontinuation/ withdrawal, whichever is earlier), is derived as follows (summing across all instances): • For Q4W arm participants requiring oral lead-in: ○ Length of time (in days) until next injection from date of dosage deviation (e.g. 2 mL administered instead of 3mL for Week 4B injection, 1ml administered instead of 2 mL for post Week 4B injections). ○ 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). ○ Length of time (in days) in excess beyond 35 days from last injection until start of oral bridging post Week 12 and in excess beyond 28 days for Week 8 and Week 12. • For Q4W arm participants not requiring oral lead-in: ○ Length of time (in days) until next injection from date of dosage deviation (e.g. 1 mL administered instead of 2 mL). ○ Length of time (in days) in excess beyond 35 days between injections. ○ Length of time (in days) in excess beyond 35 days from last injection until start of oral bridging post Week 12. • For Q8W arm participants requiring oral lead-in: ○ Length of time (in days) until next injection from date of dosage deviation (e.g. 2 mL administered instead of 3mL). ○ Length of time (in days) in excess beyond 63 days between injections post Week 16 and in excess beyond 56 days for Week 8 and Week 16 (e.g. missed or late injection visit). ○ Length of time (in days) in excess beyond 63 days from last injection until start of oral bridging post Week 16 and in excess beyond 56 days for Week 8 and Week 16. • For Q8W arm participants not requiring oral lead-in: ○ Length of time (in days) until next injection from date of dosage deviation (e.g. 2 mL administered instead of 3 mL). ○ Length of time (in days) in excess beyond 63 days between injections. ○ Length of time (in days) in excess beyond 63 days from last injection until

Number	Exclusion Description
	start of oral bridging post Week 16. • Interrupted days in oral study treatment (oral lead-in or oral bridging) if the oral dose has been interrupted for 3 or more consecutive days and the primary interruption reason is not adverse event or laboratory abnormality (based on the eCRF Exposure forms). 3 days will be assumed if such interrupted days are not available in the database.
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).
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).

15.2. Appendix 2: Schedule of Activities

While some assessments included in the Time and Events Table are conducted less frequently following the primary endpoint (Week 48), IM injections for participants during the Extension Phase will continue to be administered Q4W or Q8W based on original study randomization assignment.

All patients will be randomized at Day 1 to initiate either Q4 weekly or Q8 weekly administration of IM CAB LA + RPV LA. Only participants randomized from oral SOC treatment will participate in the Day 1 to Week 4 Oral CAB + Oral RPV lead-in treatment.

15.2.1. Protocol Defined Schedule of Events for Q4W Arm

Procedure	Screening Visit [a]	Maintenance Phase																			Extension Phase		Withdrawal Assesssments [y]	Long-Term Follow-up [z]
		Week																						
		Day 1	Week 4A (Oral Lead-in ONLY)[b]	Week 4B	8	12	16	20	24	28	32	36	40	44	48	52	Q4W 56-92	Q8W 56-92	96	100	Q4W After Week 100	Q8W After Week 96		
Written informed consent	X																							
Eligibility Verification (Inclusion/Exclusion Criteria)	X		X[c]																X[c]					
Randomization		X																						
Demography	X																							
Medical History[d]	X																							
Cardiovascular risk assessment[d]	X	X																						
Medication History/ Prior ART history	X																							
Syphilis serology + Reflex Rapid Plasma Reagin (RPR)	X	X																						

Procedure	Screening Visit [a]	Maintenance Phase																			Extension Phase		Withdrawal Assessments [y]	Long-Term Follow-up [z]
		Week																						
		Day 1	Week 4A (Oral Lead-in ONLY)[b]	Week 4B	8	12	16	20	24	28	32	36	40	44	48	52	Q4W 56-92	Q8W 56-92	96	100	Q4W After Week 100	Q8W After Week 96		
Symptom Directed Physical Exam and Medical Assessment[e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight, Height and BMI[f]		X													X				X				X	
Vital Signs: BP, HR, Temperature)[g]	X	X													X				X				X	
12-lead ECG [h] (triplicate at Day 1 pre-dose)	X	X													X				X				X	
CDC HIV-1 stage	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
AEs, SAEs, Concomitant Medications[i]	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

Procedure	Screening Visit [a]	Maintenance Phase																			Extension Phase		Withdrawal Assessments [y]	Long-Term Follow-up [z]
		Week																						
		Day 1	Week 4A (Oral Lead-in ONLY)[b]	Week 4B	8	12	16	20	24	28	32	36	40	44	48	52	Q4W 56-92	Q8W 56-92	96	100	Q4W After Week 100	Q8W After Week 96		
ISR Assessment for IM injections		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Columbia Suicide Severity Rating Scale (eC-SSRS) [j]	X	X		X	X		X		X		X		X		X			X	X				X	
Clinical chemistry and Hematology	X	X	X	X	X		X		X		X		X		X			X	X	X		X	X	X
Pregnancy Testing[k]	S	U	S	U	S	U	S	U	S	U	S	U	S	U	S	S	U	S	S	S	U	S	S	S
HIV-1 RNA and sample for storage (S)[l]	X	X	X	X	X		X		X		X		X		X	S		X	X	S		X	X	X
CD4+ cell count	X	X		X	X		X		X		X		X		X			X	X			X	X	X
CD8+ cell count		X							X						X				X				X	
Urinalysis[m]		X	X						X						X				X				X	

Procedure	Screening Visit [a]	Maintenance Phase																				Extension Phase		Withdrawal Assesssments [y]	Long-Term Follow-up [z]
		Week																							
		Day 1	Week 4A (Oral Lead-in ONLY)[b]	Week 4B	8	12	16	20	24	28	32	36	40	44	48	52	Q4W 56-92	Q8W 56-92	96	100	Q4W After Week 100	Q8W After Week 96		
Fasting Lab Assessment: Glucose, Cholesterol (Total, HDL and LDL) and Triglycerides[n]		X													X				X				X[o]	
Hepatitis B (HBsAg), Anti-HBc, and Anti-HBsAG, Hepatitis C (anti-HCV Ab)	X																							
PT/PTT/INR	X	X																						
PBMCs[p]		X													X				X				X	
Genetics sample[q]		X																						
PK sampling[r] (S)=Storage only				X	X	S	X	S	X	S	X	S	X	S	X	S	S	S	X	S			X	S

Procedure	Screening Visit [a]	Maintenance Phase																			Extension Phase		Withdrawal Assessments [y]	Long-Term Follow-up [z]
		Week																						
		Day 1	Week 4A (Oral Lead-in ONLY)[b]	Week 4B	8	12	16	20	24	28	32	36	40	44	48	52	Q4W 56-92	Q8W 56-92	96	100	Q4W After Week 100	Q8W After Week 96		
Oral CAB and Oral RPV Dispensation[s]		X	X																					
IP accountability (Pill Counts)[s]			X	X																				
IM treatment administration when transitioning from SOC[t]				X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
IM treatment administration when transitioning from CAB + RPV LA Q4W		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Patient Reported Outcomes[u]																								
HAT-QoL (short-form)		X							X						X								X	
HIV TSQs		X							X						X								X	
HIV TSQc [v]															X								X	
ACCEPT		X							X						X								X	

Procedure	Screening Visit [a]	Maintenance Phase																			Extension Phase		Withdrawal Assessments [y]	Long-Term Follow-up [z]
		Week																						
		Day 1	Week 4A (Oral Lead-in ONLY)[b]	Week 4B	8	12	16	20	24	28	32	36	40	44	48	52	Q4W 56-92	Q8W 56-92	96	100	Q4W After Week 100	Q8W After Week 96		
Reason for Switch or Reason for continuation [w]		X																						
Preference [x]															X								X	
PIN					X				X						X								X	
Safety Follow Up Visit: Conduct approximately 4 weeks after the last dose of IP. Required only if the participant has ongoing AEs or lab abnormalities at the last on-study visit. This visit may be conducted by telephone.																								

a. Complete all Screening assessments within 35 days. Participants may begin the Maintenance Phase as soon as all Screening assessments are complete. Participants may be rescreened once and will be assigned a new participant number. Participants transitioning from the 201585 (ATLAS) study must reach ATLAS Week 48 (at minimum) prior to initiating Screening procedures for ATLAS-2M and must reach ATLAS Week 52 (at minimum) prior to randomization in ATLAS-2M.

b. Visits Week 4a is part of the CAB + RPV Oral Lead-in period and is required only for participants transitioning from current SOC to CAB LA + RPV LA.

c. Confirmation of eligibility to continue the Maintenance Phase and eligibility to enter the Extension Phase.

d. Collect full routine medical history plus (report at Baseline visit): HIV risk factors (may be collected at a later study visit), cardiovascular risk factors (assessments include smoking status and history, family history of cardiac events), recent [≤6 months] illicit drug use, intravenous drug use, gastrointestinal disease, metabolic, psychiatric, renal, bone, and neurologic disorders.

e. Physical exams should be conducted as part of normal routine clinical care. Medical assessments include any decisions the study staff must make for participants management and/or care of participant.

f. Height collected at Baseline Day 1 only.

g. Measure vital signs after about 5 minutes of rest in a semi-supine position.

h. A 12-lead ECG will be performed after resting in a semi-supine position for at least 5 minutes. ECGs will be performed pre-dose. For participants transitioning from ATLAS, the pre-dose Week 48 ECG can also serve as the ATLAS-2M Screening ECG. ECG pre-dose will be performed in triplicate at Day 1. A 2-hour post-dose ECG will also be performed at Days 1 and Week 48 for participants receiving CAB LA + RPV LA with an allowable window of ±30 minutes.

i. Only SAEs related to study participation or to a concomitantly administered ViiV/GSK product will be collected between obtaining informed consent and administration of study drug at Day 1.

j. On Day 1, the eC-SSRS is to be administered prior to randomization. The eC-SSRS will preferably be completed at the beginning of the visit following administration of other PROs required prior to injections. The eC-SSRS is not required during the Withdrawal visit if withdrawal occurs during the Extension Phase.

k. Women of childbearing potential only. SR=serum, UR=urine. Pregnancy events will be captured starting at Day 1 following initial exposure to study drug. Urine pregnancy test performed at Day 1 prior to administration of study drug, at Week 4B, and at study visits when other blood draws are not required in order to limit needle sticks. Serum pregnancy test can substitute for urine pregnancy test if locally required but must be appropriately timed to confirm pregnancy status prior to randomization and first IM administration.

l. Week 48 and Week 96 HIV-1 RNA retest (within 4 weeks) for results > 50 c/mL will be captured as unscheduled visit. Plasma for storage samples will be used for possible future analyses.

m. A morning specimen is preferred. To assess biomarkers: urine albumin/creatinine ratio; urine protein/creatinine ratio; and urine phosphate. Urine phosphate results from visit 4a are not required by protocol to inform the safety review at visit 4b prior to receipt of initial CAB LA + RPV LA injections.

n. An overnight fast is preferred; however, a minimum of a 6-hour fast is acceptable.

o. Only collect if the Withdrawal visit occurs at Week 48 or Week 96.

p. Whole blood/PBMC collection samples may be used for virologic analyses. PBMCs will be collected at baseline Day 1, Week 48, Week 96, or Withdrawal if prior to Week 96.

q. Genetics sample should be collected only for patients who did not participate in the 201585(ATLAS) study (sample was previously collected and stored). 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 Day 1 visit.

r. One blood sample for CAB and RPV each to be collected at each PK timepoint. At Day 1, for participants from the ATLAS Q4W arm, PK samples are to be collected pre-dose relative to IM administration. At Week 4B, for participants randomized from SOC, Pre dose PK samples are to be collected: AFTER review of the PK diary to ensure that the samples are taken 20/28 hours after previous oral dose (diaries to be given at *Day 1 or W4a*); PRIOR to the final oral dose of CAB + RPV; PRIOR to the first IM injection.

s. Only for Participants entering CAB + RPV Oral Treatment

t. Participants switching to CAB LA + RPV LA will take final dose of oral lead-in regimen in the clinic at the Week 4B visit and begin injections. If possible, injections should be spaced approximately 2 cm from one another and from the site of any previous injection and or any injection site reaction. Bring RPV LA

to approximately room temperature prior to injecting. Time and location of injection (right or left) as well as needle length used will be collected in the eCRF. The first injection can be performed as soon as central lab results become available and safety parameters are reviewed.

u. All Patient Report Questionnaires/Surveys will be administered via paper instrument at the beginning of the visit before any other assessments are conducted and prior to administration of the eC-CSSRS. Conduct questionnaires/surveys at Withdrawal only if occurring at or prior to Week 48.

v. The HIV-TSQc is to be administered to all participants transitioning from ATLAS and new participants transitioning from oral SOC. For participants transitioning from ATLAS, the version of the HIV-TSQc instrument to be administered will be based on the initial randomization arm at ATLAS Day 1.

w. For patients randomized to oral SOC at Day 1 in ATLAS or new patients on SOC, the reasons for willingness to switch ART will be assessed at Day 1. For patients randomized to CAB LA + RPV LA Q4W in ATLAS, the reasons for willingness to continue long-acting ART in ATLAS-2M will be assessed at Day 1.

x. Preference Questionnaire will be administered to all participants.

y. Refer to Section 5.5 of the protocol for additional information on performing withdrawal assessments. HIV-1 RNA will be collected as Storage sample only if withdrawal assessments coincide with Week 52 or Week 100 (as per Section 5.5)

z. Participants receiving one or more injections with CAB LA and/or RPV LA will be assessed with clinic visits at months 3, 6, 9 and 12 during the Long-Term Follow-Up Phase

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

15.2.2. Protocol Defined Schedule of Events for Q8W Arm

Procedure	Screening Visit [a]	Maintenance Phase																		Extension Phase	Withdrawal Assessments [y]	Long-Term Follow-up z
		Week																				
		Day 1	Week 4A (Oral lead-in ONLY) b	Week 4B (Oral lead-in ONLY) b	8	9	16	24	32	40	41	48	56	64	72	80	88	96	100	Q8W After Week 96		
Written informed consent	X																					
Eligibility Verification (Inclusion/ Exclusion Criteria)	X		X[c]															X[c]				
Randomization		X																				
Demography	X																					
Medical History[d]	X																					
Cardiovascular risk assessment[d]	X	X																				
Medication History/ Prior ART history	X																					
Syphilis serology + reflex Rapid Plasma Reagin (RPR)	X	X																				

Procedure	Screening Visit [a]	Maintenance Phase																		Extension Phase	Withdrawal Assessments [y]	Long-Term Follow-up z
		Week																				
		Day 1	Week 4A (Oral lead-in ONLY) b	Week 4B (Oral lead-in ONLY) b	8	9	16	24	32	40	41	48	56	64	72	80	88	96	100	Q8W After Week 96		
Symptom Directed Physical Exam and Medical Assessment [e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight, Height and BMI [f]		X										X						X			X	
Vital Signs (BP, HR, Temperature) [g]	X	X										X						X			X	
12-lead ECG [h] (triplicate at Day 1 pre-dose)	X	X										X						X			X	
CDC HIV-1 stage	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
AEs, SAEs, Concomitant Medications	X i	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ISR Assessment for IM injection		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Procedure	Screening Visit [a]	Maintenance Phase																		Extension Phase	Withdrawal Assessments [y]	Long-Term Follow-up z
		Week																				
		Day 1	Week 4A (Oral lead-in ONLY) b	Week 4B (Oral lead-in ONLY) b	8	9	16	24	32	40	41	48	56	64	72	80	88	96	100	Q8W After Week 96		
Columbia Suicide Severity Rating Scale (eC-SSRS) [j]	X	X		X	X		X	X	X	X		X	X	X	X	X	X	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
Pregnancy Testing [k]	S	U	S	U	S		S	S	S	S		S	S	S	S	S	S	S	S	S	S	S
HIV-1 RNA and sample for storage (S) [l]	X	X		X	X		X	X	X	X		X	X	X	X	X	X	X	S	X	X	X
CD4+ cell count	X	X		X	X		X	X	X	X		X	X	X	X	X	X	X	X	X	X	X
CD8+ cell count		X						X				X						X			X	
Urinalysis [m]		X	X					X				X						X			X	
Fasting Labs Glucose, Cholesterol (Total, HDL and LDL) and Triglycerides [n]		X										X						X			X [o]	

Procedure	Screening Visit [a]	Maintenance Phase																		Extension Phase	Withdrawal Assessments [y]	Long-Term Follow-up [z]
		Week																				
		Day 1	Week 4A (Oral lead-in ONLY) [b]	Week 4B (Oral lead-in ONLY) [b]	8	9	16	24	32	40	41	48	56	64	72	80	88	96	100	Q8W After Week 96		
Hepatitis B (HBsAg), Anti-HBc, and Anti-HBsAG, Hepatitis C (anti-HCV Ab)	X																					
PT/PTT/INR	X	X																				
PBMCs [p]		X										X						X			X	
Genetics sample [q]		X																				
PK sampling when transitioning from SOC [r] (S)=Storage only				X	X	X	X	X	X	X	X	X	S	S	S	S	S	X	S		X	S
PK sampling when transitioning from CAB + RPV Q4W [r] (S)=Storage only		X			X	X	X	X	X	X	X	X	S	S	S	S	S	X	S		X	S
Oral CAB and Oral RPV Dispensation [s]		X	X																			

Procedure	Screening Visit [a]	Maintenance Phase																		Extension Phase	Withdrawal Assessments [y]	Long-Term Follow-up z
		Week																				
		Day 1	Week 4A (Oral lead-in ONLY) b	Week 4B (Oral lead-in ONLY) b	8	9	16	24	32	40	41	48	56	64	72	80	88	96	100	Q8W After Week 96		
IP accountability (Pill Counts)			X	X																		
IM treatment administration when transitioning from SOC [t]				X	X		X	X	X	X		X	X	X	X	X	X	X		X		
IM treatment administration when transitioning from CAB + RPV Q4W		X			X		X	X	X	X		X	X	X	X	X	X	X		X		
Patient Reported Outcomes [u]																						
HAT-QoL (short-form)		X						X				X									X	
HIV TSQs		X						X				X									X	
HIV TSQc [v]												X									X	
ACCEPT		X						X				X									X	
Reason for Switch or Reason for continuation w		X																				
Preference x												X									X	

Procedure	Screening Visit [a]	Maintenance Phase																		Extension Phase	Withdrawal Assessments [y]	Long-Term Follow-up [z]
		Day 1	Week																			
			Week 4A (Oral lead-in ONLY) [b]	Week 4B (Oral lead-in ONLY) [b]	8	9	16	24	32	40	41	48	56	64	72	80	88	96	100	Q8W After Week 96		
PIN					X			X				X									X	
Safety Follow Up Visit: Conduct approximately 4 weeks after the last dose of IP. Required only if the participant has ongoing AEs or lab abnormalities at the last on-study visit. This visit may be conducted by telephone.																						

a. Participants may be rescreened once and will be assigned a new participant number. Participants transitioning from the 201585 (ATLAS) study must reach ATLAS Week 48 (at minimum) prior to initiating Screening procedures for ATLAS-2M and must reach ATLAS Week 52 (at minimum) prior to randomization in ATLAS-2M.

b. Visits Weeks 4A and 4B are part of the CAB + RPV Oral Lead-in period and are required only for participants transitioning from current SOC to CAB LA + RPV LA.

c. Confirmation of eligibility to continue the Maintenance Phase, and eligibility to enter the Extension Phase.

d. Collect full routine medical history plus (report at Baseline visit): HIV risk factors (may be collected at a later study visit), cardiovascular risk factors (assessments include smoking status and history, family history of cardiac events), recent [≤6 months] illicit drug use, intravenous drug use, gastrointestinal disease, metabolic, psychiatric, renal, bone, and neurologic disorders.

e. Physical exams should be conducted as part of normal routine clinical care. Medical assessments include any decisions the study staff must make for participants management and/or care of participant.

f. Height collected at Baseline Day 1 only.

g. Measure vital signs after about 5 minutes of rest in a semi-supine position.

h. A 12-lead ECG will be performed after resting in a semi-supine position for at least 5 minutes. ECGs will be performed pre-dose. For participants transitioning from ATLAS, the pre-dose Week 48 ECG can also serve as the ATLAS-2M Screening ECG. ECG pre-dose will be performed in triplicate at Day 1. A 2-hour post-dose ECG will also be performed at Days 1 and Week 48 for participants receiving CAB LA + RPV LA with an allowable window of ± 30 minutes.

i. Only SAEs related to study participation or to a concomitantly administered ViiV/GSK product will be collected between obtaining informed consent and administration of study drug at Day 1.

j. On Day 1, the eC-SSRS is to be administered prior to randomization. The eC-SSRS will preferably be completed at the beginning of the visit following administration of other PROs required prior to injections. The eC-SSRS is not required during the Withdrawal visit if withdrawal occurs during the Extension Phase.

k. Women of childbearing potential only. SR=serum, UR=urine. Pregnancy events will be captured starting at Day 1 following initial exposure to study drug. Serum pregnancy test can substitute for urine pregnancy test if locally required but must be appropriately timed to confirm pregnancy status prior to randomization and first IM administration.

l. Week 48 and Week 96 HIV-1 RNA retest (within 4 weeks) for results > 50 c/mL will be captured as unscheduled visit. Plasma for storage samples will be used for possible future analyses.

m. A morning specimen is preferred. To assess biomarkers: urine albumin/creatinine ratio; urine protein/creatinine ratio; and urine phosphate. Urine phosphate results from visit 4a are not required by protocol to inform the safety review at visit 4b prior to receipt of initial CAB LA + RPV LA injections.

n. An overnight fast is preferred; however, a minimum of a 6-hour fast is acceptable.

o. Only collect if the Withdrawal visit occurs at Week 48 or Week 96.

p. Whole blood/PBMC collection samples may be used for virologic analyses. PBMCs will be collected at baseline Day 1, Week 48, Week 96, or Withdrawal if prior to Week 96.

q. Genetics sample should be collected only for patients who did not participate in the 201585(ATLAS) study (sample was previously collected and stored). 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 Day 1 visit.

r. One blood sample for CAB and RPV each to be collected at each PK timepoint. At Day 1, for participant from the ATLAS Q4W arm, PK samples are to be collected pre-dose relative to IM administration. injection. At Week 4B, for participants randomized from SOC, Pre dose PK samples are to be collected: AFTER review of the PK diary to ensure that the samples are taken 20/28 hours after previous oral dose (diaries to be given at Day 1 or W4a); PRIOR to the final oral dose of CAB + RPV; and PRIOR to the first IM injection. At Week 9 and 41, the PK samples should be collected 3 to 10 days after the Week 8 and Week 40 visits, respectively.

s. Only for Participants entering CAB + RPV Oral Treatment

t. Participants switching to CAB LA + RPV LA will take final dose of oral lead-in regimen in the clinic at the Week 4B visit and begin injections. If possible, injections should be spaced approximately 2 cm from one another and from the site of any previous injection and or any injection site reaction. Bring RPV LA to approximately room temperature prior to injecting. Time and location of injection (right or left) as well as needle length used will be collected in the eCRF. The first injection can be performed as soon as central lab results become available and safety parameters are reviewed.

u. All Patient Report Questionnaires/Surveys will be administered via paper instrument at the beginning of the visit before any other assessments are conducted and prior to administration of the eC-CSSRS. Conduct questionnaires/surveys upon Withdrawal only if occurring at or prior to Week 48

v. The HIVTSQc is to be administered to all participants transitioning from ATLAS and new participants transitioning from oral SOC. For participants transitioning from ATLAS, the version of the HIV-TSQc instrument to be administered will be based on the initial randomization arm at ATLAS Day 1

w. For patients randomized to oral SOC at Day 1 in ATLAS or new patients on SOC, the reasons for willingness to switch ART will be assessed at Day 1. For patients randomized to CAB LA + RPV LA Q4W in ATLAS, the reasons for willingness to continue long-acting ART in ATLAS-2M will be assessed at Day 1.

x. Preference Questionnaire will be administered to all participants

y. Refer to Section 5.5 of the protocol for additional information on performing withdrawal assessments. HIV-1 RNA will be collected as Storage sample only if withdrawal assessments coincide with Week 52 or Week 100 (as per Section 5.5)

z. Participants receiving one or more injections with CAB LA and/or RPV LA will be assessed with clinic visits at months 3, 6, 9 and 12 during the Long-Term Follow-Up Phase

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

15.3. Appendix 3: Assessment Windows

15.3.1. Definitions of Assessment Windows for Analyses

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

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

For parameters which are not scheduled to be assessed at particular visits, the all-inclusive assessment windows will still be used; however, data summaries will only report scheduled visits. Assessments at unscheduled visits will be included for 'any time On-treatment' time points and in data listings, as well any algorithms that make use of additional data (e.g., Snapshot).

Prior to visit slotting, assessments are first assigned to a study phase (screening, maintenance, extension, or long-term follow-up) based on the Tables in Section 15.4.1 and treatment state based on Section 15.4.2.

Maintenance phase assessments other than health outcome and PK are assigned based on the Study Day as shown in Table 8 and Table 10. Table 8 also includes visiting slotting for screening assessments. 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 other than health outcome and PK are assigned based on the Study Day as shown in Table 9. 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).

Long-term Follow-up phase assessments are assigned based on the LTFU study day as shown in

Table 11. The analysis visits in LTFU should be only applied to the assessments that are already assigned to LTFU phase regardless of treatment state. See Section 15.6.1, for derivation of Study Day and LTFU Study Day.

15.3.2. Definitions of Assessment Windows for Analyses other than Health Outcome and PK

Table 8 Assessment Windows for Screening and Maintenance Phase Data

All Parameters except for where noted[c]	Target Study Day	Analysis Window	Analysis Timepoint
	The study day of first record	Study Day ≤ 1	Screening
	1	Last available recorded value up to and including the Maintenance treatment start date, excluding 2-hour post-dose ECG taken on the Maintenance treatment start date	Baseline
Urinalysis[a]	29	2 ≤ Study Day ≤ 70	Week 4
		2 ≤ Study Day ≤ 42, including 2-hour post-dose ECG taken on Maintenance treatment start date	
	57	43 ≤ Study Day ≤ 84	Week 8
	113	85 ≤ Study Day ≤ 140	Week 16
Urinalysis[a], CD8, CD4/CD8 ratio	169	141 ≤ Study Day ≤ 210	Week 24
		141 ≤ Study Day ≤ 196	
	225	197 ≤ Study Day ≤ 252	Week 32
	281	253 ≤ Study Day ≤ 308	Week 40
Urinalysis[a], fasting glucose, lipids[b], CD8, CD4/CD8 ratio, weight, vital signs, ECG	337	309 ≤ Study Day ≤ 378	Week 48
		309 ≤ Study Day ≤ 364	
	393	365 ≤ Study Day ≤ 420	Week 56
	449	421 ≤ Study Day ≤ 476	Week 64
	505	477 ≤ Study Day ≤ 532	Week 72
	561	533 ≤ Study Day ≤ 588	Week 80
	617	589 ≤ Study Day ≤ 644	Week 88
Urinalysis[a], fasting glucose, lipids[b], CD8, CD4/CD8 ratio, weight, vital signs, ECG	673	645 ≤ Study Day ≤ 714	Week 96
		645 ≤ Study Day ≤ 686	
	701	687 ≤ Study Day ≤ (Study Day of Nominal Week 100 visit)	Week 100
If a participant permanently discontinued study treatment:			
		For Participants on Q8W Arm: Date > max (Date of Last Oral Dose of CAB+RPV + 1, Date of	Follow-up

All Parameters except for where noted[c]	Target Study Day	Analysis Window	Analysis Timepoint
		Last Injection + 63) **For Participants on Q4W Arm:** Date > max (Date of Last Oral Dose of CAB+RPV + 1, Date of Last Injection + 35)	

NOTES:
- The nominal Week 100 visit refers to the Week 100 visit per eCRF.
- Follow-up will be derived only for participants who permanently discontinued study treatment.

[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] **Lipids**: Cholesterol, HDL Cholesterol Direct, LDL Cholesterol Calculation, LDL Cholesterol Direct, Total Cholesterol/HDL Cholesterol Ratio, Triglycerides
[c] Analysis windows for parameters with sparse collection are noted.

Table 9 Assessment Windows for Extension Phase Data

Parameter (if applicable)	Target Study Day	Analysis Window	Analysis Timepoint
All	729	(Study Day of Nominal Week 100 visit + 1) ≤ Study Day ≤ 756	Week 104
	785	757≤ Study Day ≤ 812	Week 112
	841	813≤ Study Day ≤868	Week 120
	7*w + 1	(7*w - 27) ≤ Study Day ≤ (7*w + 28)	Week w w = 128, 136,…
If a participant permanently discontinued study treatment:			
		For participants on Q8W Arm: Date > max (Date of Last Oral Dose of CAB+RPV + 1, Date of Last Injection + 63)	Follow-up
		For participants on Q4W Arm: Date > max (Date of Last Oral Dose of CAB+RPV + 1, Date of Last Injection + 35)	

NOTES:
- The nominal Week 100 visit refers to the Week 100 visit per eCRF.
- Follow-up will be derived only for participants who permanently discontinued study treatment.

Table 10 Assessment Windows for Summary of Snapshot Data — Data Assigned to Maintenance Phase Only

Snapshot Analysis Windows (If no on-treatment viral load data in default window, use expanded window)		Analysis Timepoint
Default	**Expanded +6 Week Upper Window[a]**	
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	Baseline
2 ≤ Study Day ≤ 42	2 ≤ Study Day ≤ 70	Week 4
43 ≤ Study Day ≤ 84	43 ≤ Study Day ≤ 98	Week 8
85 ≤ Study Day ≤ 140	85 ≤ Study Day ≤ 154	Week 16
141 ≤ Study Day ≤ 196	141 ≤ Study Day ≤ 210	Week 24
197 ≤ Study Day ≤ 252	197 ≤ Study Day ≤ 266	Week 32
253 ≤ Study Day ≤ 308	253 ≤ Study Day ≤ 322	Week 40
295 ≤ Study Day ≤ 378	295 ≤ Study Day ≤ 378	Week 48
365 ≤ Study Day ≤ 420	365 ≤ Study Day ≤ 434	Week 56
421 ≤ Study Day ≤ 476	421 ≤ 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:

- For post-baseline visits (i.e. Week 4 and afterwards), apply Snapshot analysis windows only to viral load data that is on-treatment (per Table 16) within the Maintenance Phase (per Table 14).
- An on-treatment viral load assessment may be assigned to more than one snapshot analysis window, e.g. on-treatment assessment taken on Study Day 300 will be in both Week 40 and Week 48.

a. ± 6 Week window is always used at key analysis timepoints (Week 48 and Week 96). For analysis timepoint of Week 24, if no viral load data in default window, expand to ± 6 Week window, i.e. (127 ≤ Study Day ≤ 210) in Week 24 IDMC and Week 24 Analyses, and expand upper bound to +6 weeks in all other analyses.

Table 11 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 Study Treatment

Analysis Window	Analysis Timepoint	Target Study Day of Window
1 ≤ LTFU Study Day ≤ 63	LTFU Month 1/WD[a]	30
64 ≤ LTFU Study Day ≤ 135	LTFU Month 3	90
136 ≤ LTFU Study Day ≤ 225	LTFU Month 6	180
226 ≤ LTFU Study Day ≤ 315	LTFU Month 9	270
316 ≤ LTFU Study Day ≤ 405	LTFU Month 12	360
(30*m - 44) ≤ LTFU Study Day ≤ (30*m + 45)	LTFU Month m m = 15, 18,21,…	7*m

NOTES:

- An assessment may be assigned to both LTFU and maintenance/extension phases.

a. For participants who receives at least one injection of CAB+RPV and permanently discontinues study treatment, they will not complete withdrawal visit, will instead move directly into the LTFU and have LTFU Month 1 visit as the first planned LTFU visit per protocol amendment 1; however, per protocol amendment 2, they will complete withdrawal visit and then have LTFU Month 3 visit as the first planned LTFU visit. Data have been collected either per protocol amendment 1 or per protocol amendment 2 and are included in the database. The analysis timepoint of LTFU Month 1/WD is intended for slotting data mainly collected from either

Analysis Window	Analysis Timepoint	Target Study Day of Window
LTFU Month 1 visit per protocol amendment 1 or withdrawal visit per protocol amendment 2 if the date of assessments or onset date of event falls within the specified analysis window.		

15.3.3. Assessment Window for Phase Conclusion

The 'Phase Conclusion' records in disposition data will be slotted based on Table 8 (for Maintenance Phase conclusion records) and Table 9 (for Extension Phase conclusion records). However, if the discontinuation date is post-treatment per Table 16, the record will be slotted to the last on-treatment visit within the same phase rather than follow up.

15.3.4. Assessment Window for Health Outcome Data

15.3.4.1. PIN / HAT-QoL / HIVTSQs / HIVTSQc / ACCEPT / Preference

PIN, HAT-QoL, HIVTSQs, HIVTSQc, ACCEPT and Preference questionnaire assessments will be assigned to analysis visits as follows:

1. Baseline will be defined as last available recorded value up to and including the Maintenance treatment start date (expected to be collected at Day 1). Baseline is not applicable for PIN, HIVTSQc and Preference assessments.
2. For post-baseline visits, if the nominal visit identifier as captured in the source dataset corresponds to a scheduled collection per the Time and Events Schedule (see Section 15.2 and Table 12) and the assessment is collected in the Maintenance Phase (per Table 14), then the nominal visit identifier will be kept as the analysis visit.
3. For post-baseline visits, 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 14. 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 Day 1, Week 24, and 48. 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 15.3.6.

Table 12 Planned Nominal Visit of Health Outcome Data

Questionnaire	Day 1	Week 8	Week 24	Week 48
PIN		x	x	x
HAT-QoL	x		x	x
HIVTSQs	x		x	x
HIVTSQc				x
ACCEPT	x		x	x
Preference				x
NOTES: Day 1 visits are recorded as "Baseline" visits in the database.				

15.3.4.2. Reasons for Continuation/Switch

Reasons for Continuation/Switch assessments are planned to be taken at nominal Baseline (Day 1) visit only. The assessments taken within ± 2 weeks window from maintenance phase treatment start date will be regarded as evaluable. The assessments taken outside this window will be excluded from the summary.

15.3.5. Assessment Window for PK Concentration Data

For PK concentration data at the withdrawal/unscheduled/LTFU Month 1visits during maintenance phase (after assignment to study phase per Table 14), the visit will be slotting to the analysis visit per the following steps:

- Identify the 'last nominal visit' with the PK pre-dose assessment performed prior to the visit to be slotted during the same study phase
- Identify the nominal visit corresponding to the next planned pre-dose PK assessment visit (excluding visits with storage PK collection), that is subsequent to the 'last nominal visit' with PK pre-dose assessment during the same study phase.
- If the nominal visit corresponding to next planned pre-dose PK assessment visit is prior to/at Week 48 visit, the PK assessment at the unscheduled/withdrawal/LTFU Month1 visit will be slotted to this nominal visit corresponding to next planned pre-dose PK assessment visit.
- Otherwise, the PK assessment at 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
    - The nominal visit of the next planned injection occurring on or after the date of the PK assessment during the same study phase

During maintenance phase, the planned nominal visits for PK Pre-dose are Week 4B, 8, 16, 24, 32, 40, 48, 96 for Q4W arm; and are Day 1, Week 4B, 8, 16, 24, 32, 40, 48, 96 for

Q8W arm while Day 1 is required only for those transitioning from ATLAS on Q4W injections and Week 4B is required only for participants transitioning from oral SOC and requiring oral CAB+RPV lead-in. In addition, the participants on Q8W arm have planned nominal visits at Week 9 and 41 for 1-week post-dose.

For participants requiring oral CAB+RPV lead-in, the planned injection visits are Week 4B, Week 8, continuing every 4 weeks for Q4W arm and continuing every 8 weeks for Q8W arm. For participants not requiring oral CAB+RPV lead-in, the planned injection visits are every 4 weeks starting from Day 1 for Q4W arm and every 8 weeks starting from Day 1 for Q8W arm.

Example 1: If a participant on Q8W arm has the 'last nominal visit' (with PK pre-dose assessment) at Week 24 and then withdraws around Week 28, with the last injection at Week 24 and a Maintenance Phase PK assessment labelled at 'LTFU Month 1'., This PK assessment labelled as 'LTFU Month 1' will be slotted to the subsequent planned nominal visit of Week 32.

Example 2: If a participant on Q4W arm has the 'last nominal visit' (with PK pre-dose assessment) at Week 48 and then have an unscheduled Maintenance Phase PK assessment around Week 74. This assessment will be slotted to the next planned injection visit, Week 76.

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

15.3.6. Multiple Assessments within an Assessment Window

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

For data other than health outcome/PK concentration:

1. the assessment closest to the window target Study Day;
2. if there are multiple assessments equidistant from the target Study Day, then the mean of these values will be used. For HIV-1 RNA, the geometric mean of the number of copies will be used as opposed to the arithmetic mean.

For Health outcome 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 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 originates 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 valid 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, LOCF or CVF identification).

15.4. Appendix 4: Study Phases and Treatment State

15.4.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to the Treatment Start Date defined in Section 15.6.1.

AEs will be assigned to study phases as defined in Table 13. For example, adverse events on/after start of maintenance phase IP and prior to start of Extension phase IP/LTFU ART will be assigned to the Maintenance Phase.

Laboratory data (efficacy, safety, PK and virology), HIV associated Conditions, health outcomes assessments, vital signs, and ECGs will be assigned to study phases as defined as in Table 14. For example, assessments/events occurring after start of maintenance phase IP and 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. No study phases will be assigned to medications.

Table 13 Assignment of Study Phases for AEs

Study Phase	Definition
Screening	Date < Maintenance Treatment Start Date
Maintenance	**For participants continuing into Extension Phase:** Maintenance Treatment Start Date ≤ Date < Date of Nominal Week 100 Visit **For participants not continuing into Extension Phase[a]:** Maintenance Treatment Start Date ≤ Date < LTFU ART Start Date For AEs leading to withdrawal and started on the same date as LTFU ART Start Date, Maintenance Phase, instead of Long-term Follow-up phase, will be assigned.
Extension	**Participants continuing into Extension Phase[a]:** Date of Nominal Week 100 Visit ≤ Date < LTFU ART Start Date For AEs leading to withdrawal and started on the same date as LTFU ART Start Date, Extension Phase, instead of Long-term Follow-up phase, will be assigned.

NOTES:
- Date = AE Start date
- [a] If participants have missing LFTU ART start date, only the lower bound will be considered in the derivation.

Table 14 Assignment of Study Phases for Lab Assessments (including PK and Virology), ECG, Protocol Deviations, Vital Sign, Health Outcomes, HIV Associated Conditions

Study Phase	Definition
Screening	Date ≤ Maintenance Treatment Start Date Note: 2-hour post-dose ECG taken on the Maintenance Treatment Start Date will be excluded.
Maintenance	**For participants continuing into Extension Phase:** Maintenance Treatment Start Date < Date ≤Date of Nominal Week 100 Visit Note: 2-hour post-dose ECG taken on the Maintenance Treatment Start Date will be included. **For participants not continuing into Extension Phase[a]:** Maintenance Treatment Start Date < Date ≤ LTFU ART Start Date Note: 2-hour post-dose ECG taken on the Maintenance Treatment Start Date will be included.
Extension	**Participants continuing into Extension Phase[a]:** Date of Nominal Week 100 Visit < Date ≤ LTFU ART Start Date

- Date = start or assessment date
- [a] If participants have missing LFTU ART start date (i.e. the participants have not started ART in LFTU yet), only the lower bound of the window will be considered in the derivation.

Table 15 Assignment to Long-term Follow-up Phase

Study Phase	Definition
Long-term Follow-up	Date > max (Last IM Injection Date, Last Oral Bridging End Date)

- Date = Assessment/Start Date
- For AEs leading to withdrawal and started on the same date as LTFU ART Start Date, maintenance phase or extension phase depending on participant's continuation status to extension phase, instead of long-term follow-up phase, will be assigned. Refer to Table 13 for details.

Only participants who received at least one CAB and/or RPV injection will enter the long-term follow-up. 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.

15.4.2. Treatment State

Within each treatment study phase (i.e. Maintenance and Extension—based on assignment of study phase described in Section 15.4.1), only those assessments which occur within the ranges shown in Table 16 will be considered 'on-treatment' for the given phase. No treatment states will be assigned to medications.

Table 16 Treatment State within Study Phases[b]

Study Phase[a]	Treatment State	Date Range
Screening	Pre-treatment	All assessments/events within the phase
Maintenance	On-treatment	Q8W arm: Date ≤ max (Date of Last Injection + 63, Date of Last Dose of Oral CAB+RPV + 1)
		Q4W arm: Date ≤ max (Date of Last Injection + 35, Date of Last Dose of Oral CAB+RPV + 1)
	Post-treatment	Q8W arm: Date > max (Date of Last Injection + 63, Date of Last Dose of Oral CAB+RPV + 1)
		Q4W arm: Date > max (Date of Last Injection + 35, Date of Last Dose of Oral CAB+RPV + 1)
Extension	On-treatment	Q8W arm: Date ≤ max (Date of Last Injection + 63, Date of Last Dose of Oral CAB+RPV + 1) Q4W arm: Date ≤ max (Date of Last Injection + 35, Date of Last Dose of Oral CAB+RPV + 1)
	Post-treatment	Q8W arm: Date > max (Date of Last Injection + 63, Date of Last Dose of Oral CAB+RPV + 1) Q4W arm: Date > max (Date of Last Injection + 35, Date of Last Dose of Oral CAB+RPV + 1)
Long-term Follow-up	On-treatment	Q8W arm: Date ≤ min (LTFU ART start date, max (Date of Last Injection + 63, Date of Last Dose of Oral CAB+RPV + 1)) Q4W arm: Date ≤ min (LTFU ART start date, max (Date of Last Injection + 35, Date of Last Dose of Oral CAB+RPV + 1))
	Post-treatment	Q8W arm: Date > min (LTFU ART start date, max (Date of Last Injection + 63, Date of Last Dose of Oral CAB+RPV + 1)) Q4W: Date > min (LTFU ART start date, max (Date of Last Injection + 35, Date of Last Dose of Oral CAB+RPV + 1))

NOTE:

- Date = Assessment/Start Date.

a. Treatment State is determined after data has been assigned to the study phases as defined in Section 15.4.1.

b. Last injection and/or last dose of oral CAB+RPV are only applied to participants who permanently discontinued the study treatment. The assessments for participants who did not permanently discontinue the study treatment will be considered 'On-treatment'. For participants continuing into extension phase, all data assigned to maintenance phase per Section 15.4.1 will be considered 'On-treatment'.

15.4.2.1. Treatment States for AE Data

For adverse events, partial AE start date will use imputation as described in Section 15.7.2.1. In the case of a completely missing start date, the event will be considered to have started On-treatment in the 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.

Additional variables will be derived as shown in Table 17.

Table 17 Days since First Dose of Each Study Phase, Days since Phase Start, AE Duration and Relation to Study Treatment

	Definition
Days since First Dose (Days)[a]	AE Start Date – Maintenance Treatment Start Date + 1
Days since Last Dose (Days)[a]	AE Start Date – Date of Last Dose of Study Treatment prior to/on the Start Date of AE + 1
Days since Phase Start	**For AEs in Maintenance Phase:** AE Start Date - Maintenance Treatment Start Date + 1 **For AEs in Extension Phase:** AE Start Date – Date of Nominal Week 100 Visit + 1 **For AEs in Long-term Follow-up Phase:** AE Start Date – Date of Last Dose of Study Treatment[b]
Duration (Days)	AE Resolution Date – AE Start Date + 1
Drug-related	If relationship is marked 'YES' on Inform/eCRF or value is missing.

NOTES:

a. Days since First/Last Dose will only be derived for AEs assigned to maintenance phase, extension phase and long-term follow-up phase.

b. Date of Last Dose of Study Treatment = max (Last IM Injection Date, Last Oral Bridging End Date), only applicable to participants who permanently discontinued study treatment.

15.4.3. Study Period

Certain displays will be produced for data collected during the oral lead-in. The study period variable is defined in Table 18 and Table 19. Study period is assigned after the study phase is assigned (screening, maintenance, extension, or long-term follow-up) based on the Tables in Section 15.4.1.

Table 18 Assignment of Study Period for AE Data

Study Period	Date range
Oral Lead-in	**For participants receiving at least one Injection:** Maintenance Treatment Start Date ≤ Date < Date of First IM Injection **For participants withdrawing prior to first Injection:** Date ≥ Maintenance Treatment Start Date Note that the oral lead-in period is only applicable to the participants who received at least one dose of study treatment during the oral lead-in period in the study. Oral lead-in period is within the maintenance phase.

NOTES:
- Date = AE Start date.

Table 19 Assignment of Study Period for Lab Assessments:

Period	Date range
Oral Lead-in	**For participants receiving at least one Injection:** Maintenance Treatment Start Date < Date ≤ Date of First IM Injection **For participants withdrawing prior to first Injection:** Date > Maintenance Treatment Start Date Note that the oral lead-in period is only applicable to the participants who received at least one dose of study treatment during the oral lead-in period in the study. Oral lead-in period is within the maintenance phase.

NOTES:
- Date = Date of assessment.

15.5. Appendix 5: Data Display Standards & Handling Conventions

15.5.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: us1salx00259
HARP Compound	: \ARPROD\GSK1265744\mid207966
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.0). • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM.	
Generation of RTF Files	
• RTF files will be generated for every reporting effort described in the RAP.	

15.5.2. Reporting Standards

General

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

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

• Reporting for tables, figures and formal statistical analyses:
  ○ Actual time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  ○ The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.
• Reporting for Data Listings:
  ○ If space allows, planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1).
  ○ Unscheduled or unplanned readings will be presented within the participant's listings.

○ When data falls within both maintenance / extension and long-term follow-up phases, it will be presented in maintenance / extension phase, unless otherwise specified. ○ Unless otherwise specified, when data falls within both screening and baseline visits per analysis visit windows, it will be presented at baseline visit.
Unscheduled Visits
• Unscheduled visits will be assigned to a study visit using the all-inclusive windows defined in Section 15.3. • However, data summaries will only report visits that are planned assessment time points for each parameter (according to the Time and Events table). • Assessments at unscheduled visits will be included for 'any time On-treatment' time points and in data listings, as well any algorithms that make use of additional data (e.g., Snapshot).
Descriptive Summary Statistics
Continuous Data: Refer to IDSL Statistical Principle 6.06.1
Categorical Data: N, n, frequency, %
Graphical Displays
• Refer to IDSL Statistical Principals 7.01 to 7.13.

15.5.3. Reporting Standards for Pharmacokinetic

Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Refer to IDSL Statistical Principle 6.06.1 Assign the low limit of quantification (CAB 0.025 ug/mL, RPV 1 ng/mL) to NQ values.
Reporting of Pharmacokinetic Parameters	
Descriptive Summary Statistics (Log_e Transformed)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of log_e transformed data and between participant coefficient of variation (CV_b (%)) will be reported. ○ $CV_b(\%) = \sqrt{\exp(SD^2) - 1} \times 100$ (SD = SD of log_e transformed data)

15.6. Appendix 6: Derived and Transformed Data

15.6.1. General

Multiple Measurements at One Time Point
• If after window assignment there are multiple valid assessments of a parameter within the same window, refer to Section 15.3.6 for determination of the value to be used for summary statistics of observed values. Assessments not chosen for use in summary statistics will still appear in the associated listings. Assessments not chosen for use in summary statistics by this algorithm will still appear in the associated listings. Also, all applicable valid 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, LOCF or CVF identification).
Treatment Start Date
Treatment start date is defined as follows: Maintenance Phase • Date of first ATLAS-2M dose of CAB+RPV (oral or injection) entered onto the IP exposure eCRF form. Extension Phase • For participants not continuing into extension phase, treatment start date is missing. • For participants continuing into extension phase, treatment start date is the date of first dose of CAB+ RPV (oral or injection) at or after nominal Week 100 visit. Long-term Follow-up Phase • If a participant is still on study treatment, or permanently discontinued the study treatment and did not have any previous injections, treatment start date is missing. • If a participant permanently discontinued the study treatment and had at least one injection, treatment start date is the date of first ART treatment after the last dose of study treatment (oral or injection).
Study Day

The Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the start date of study treatment during the Maintenance Phase as follows:
 	
if date of event ≥ start date of study treatment, then
• $\text{Study Day} = \text{date of event} - \text{start date of Maintenance Phase treatment} + 1$
 	
if date of event < start date of study treatment, then
• $\text{Study Day} = \text{date of event} - \text{start date of Maintenance Phase treatment}$
 	
Note that the start date of study treatment during 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 Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the date of nominal Week 100 visit as follows:
if date of event ≥ date of nominal Week 100 visit, then
• Study Day=date of event - date of nominal Week 100 visit + 1
 	
if date of event < date of nominal Week 100 visit, then
• Study Day = date of event − date of nominal Week 100 visit
 	
Note that the date of nominal Week 100 visit is considered to be on Extension Phase Study Day 1 and the day before this is Extension Phase Study Day -1; i.e., there is no Extension Phase Study Day 0.

Long-term Follow-up Study Day
The Long-Term Follow Up (LTFU) Study Day of an event (e.g., lab assessment, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the end of IP treatment [i.e. max(Last IM Injection Date, Last Oral Bridging End Date)] as follows: If the date of event falls in Long-term Follow up phase, then • LTFU Study Day = Date of Event - End Date of IP
Change from Baseline
• Post-Dose Visit Value – Baseline   ○ Unless otherwise specified, the baseline definitions specified in Section 5.2 will be used for derivations for endpoints / parameters.

15.6.2. Study Population

Demographics and Baseline Characteristics
Age
• Age, in whole years, will be calculated with respect to the participant's Screening visit. • GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows: ○ Any participant with a missing date and month will have this imputed as '30th June'. • Birth date will be presented in listings as 'YYYY'. • Completely missing dates of birth will remain as missing, with no imputation applied. Consequently, the age of the participant will not be calculated and will remain missing.
Body Mass Index (BMI)
• Calculated as Weight (kg) / Height $(m)^2$
Hepatitis Status
• Hepatitis C status will be determined using antibody 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., ≥ limit of quantification) or not. • A participant will be considered positive for hepatitis B virus (HBV) if they have a positive

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surface antigen or detectable HBV DNA result. "HBV DNA DETECTED" in the lab comment takes precedence over HBV DNA test result for positive hepatitis B status, for example, if a participant has HBV test result below level of detection, however, the lab comment shows that HBV DNA detected, this participant will be considered positive for hepatitis B. If HBV DNA result is available, it will be used to qualify hepatitis B status as positive or negative (positive if ≥ limit of quantification); otherwise Hepatitis B status will be determined using the surface antigen result.

- Hepatitis status at entry will be based on the assessments prior to/on the start of the study treatment.

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 et al. 2008] is

For females:

$$\hat{p}_F = 1 - S_0(t)^{\exp\left\{\begin{array}{c}2.32888\times\log(age)+1.20904\times\log(TC)-0.70833\times\log(HDL)+2.76157\times\log(SBP_u)+\\ 2.82263\times\log(SBP_t)+0.52873\times I_s+0.69154\times I_d-26.1931\end{array}\right\}}$$

For males:

$$\hat{p}_M = 1 - S_0(t)^{\exp\left\{\begin{array}{c}3.06117\times\log(age)+1.12370\times\log(TC)-0.93263\times\log(HDL)+1.93303\times\log(SBP_u)+\\ 1.99881\times\log(SBP_t)+0.65451\times I_s+0.57367\times I_d-23.9802\end{array}\right\}}$$

where

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

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

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

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)

- 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 Day 1. A current smoker is defined as currently smoking/using tobacco or has smoked/used tobacco within the previous 6 months; a former smoker is defined as previously smoked/used tobacco products and has not smoked/used

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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 they will be counted in the highest category of risk in the summary by category.
Prior Exposure to CAB+RPV
• For participants transitioning from ATLAS study and having prior exposure to CAB+RPV in ATLAS study: Duration of Prior Exposure to CAB+RPV = Randomization Date – Prior Oral CAB Start Date in ATLAS Study + 1. • For participants transitioning from ATLAS study and not having prior exposure to CAB+RPV in ATLAS study, or for participants randomized from current SOC, Duration of Prior Exposure to CAB+RPV = 0. • Duration of Prior Exposure to CAB+RPV will be categorized to 0 weeks, 1-24 weeks and >24 weeks.
Lipid-modifying Agents
• The following ATC codes correspond to lipid-modifying agents: o ATC Level 2: C10 o ATC Level 3: C10A, C10B (if Level 2 is not available) o ATC Level 4: C10AA, C10AB, C10AC, C10AD, C10AX, C10BA, C10BX (if level 2, 3 are not available) • 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.

15.6.3. 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 10) is typically determined by the last available HIV-1 RNA measurement in that window while the participant is On-treatment in the Maintenance Phase (as assigned based on Section 15.4). • 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 ‘HIV-1 RNA < 50 c/mL’ or reported as ‘No Virologic Data at Week X’; in the latter case, the algorithm further classifies the nature of the missing data. Typically, a 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 categorized as ‘HIV-1 RNA ≥ 50 c/mL’. • Full details of the algorithm, including the handling of special cases, are included in Section 15.9

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 Not 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 Not Detected" or "Target Detected" will be captured in the database. • Super low viral load will also be tested by BioMNTR lab for viral loads below the limit of quantification at some visits (e.g. Week 48).
Confirmed Virologic Failure (CVF)
• The definition of CVF is provided in the Protocol, Section 5.5.4 – Definition of Confirmed Virologic Failure. • In case there are multiple plasma HIV-1 RNA results on the same day, the worst result (i.e. the largest value) will be used in determination of CVF.
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 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 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 time point of interest 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 10: Variables Defined for Time to Event Analysis for additional details.
Summary for Participants per Viral Load Category by Visit

• Summary will be based on observed available data, with no imputation for missing values. The proportion of participants in each viral load category will be calculated using the denominator and numerator specified below:
  ○ Denominator: Number of participants with on-treatment viral load within the snapshot visit window.
  ○ Numerator: Number of participants with plasma HIV-1 RNA in the specified category based on the last on-treatment viral load assessment collected within the snapshot visit window.

HIV-1 Disease progression Stage

- Categories:
  - CDC Stage I at Baseline to CDC Stage III;
  - CDC Stage II at Baseline to CDC Stage III;
  - CDC Stage III at Baseline to new CDC Stage III event;
  - CDC Stage I, II, III at Baseline to Death.

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

- For the purpose of analysis, the CDC at Baseline and at post-baseline during Maintenance Phase will be derived as below:
  - At Baseline, the 'Baseline CDC stage' for each participant was assessed by investigator and recorded in the eCRF. However, for the analysis, Baseline CDC stage will be rederived based Baseline CD4+ values as well as whether any HIV-associated/AIDS-defining conditions present at baseline per the Criteria's thresholds (Appendix 4 in Protocol).
  - To analyse disease progression, the most advanced post-baseline CDC stage within the period of interest (e.g. Maintenance Phase) will be derived based on the occurrences of new AIDs-defining conditions (please refer to Appendix 4 in Protocol for the list of AIDs-defining Conditions) as well as the nadir value of post-baseline CD4+.
    - For example, if a participant with CDC 'Stage I' at Baseline had the lowest Maintenance Phase CD4+ =120 cell/mm^3 without new AIDs-defining conditions, then HIV disease progression for this participant during the Maintenance Phase would be considered as 'CDC stage I at Baseline to CDC stage III'.
    - If a participant with CDC 'Stage II' at Baseline 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 during the Maintenance Phase would be considered as 'CDC stage II at Baseline to CDC stage III'.

Delay in IP Injection

- For participants on the Q4W arm, IM dosing is expected to occur every 4 weeks from Week 4B onwards for those transitioning from SOC (i.e. those requiring oral lead-in) and from Day 1 onwards for those transitioning from CAB+RPV Q4W in ATLAS (i.e. those not requiring oral lead-in). The Delay in IP injection (days) will be calculated as:

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

- For participants on the Q8W arm, IM dosing is expected to occur at Week 4B and then every 8 weeks from Week 8 onwards for those transitioning from SOC (i.e. those requiring oral lead-in) and every 8 weeks from Day 1 for those transitioning from CAB+RPV Q4W (i.e. those not requiring oral lead-in) in ATLAS.
  - For participants transitioning from SOC on the Q8W arm, if the preceding injection occurs at Week 4B, the Delay in IP injection (days) will be calculated as:
    Delay in IP Injection (days) = Date of Week 8 injection - date of Week 4B injection - 28 days
  - For participants transitioning from SOC on the Q8W arm, if the preceding injection occurs at a visit later than Week 4B, the Delay in IP injection (days) will be calculated as:
    Delay in IP Injection (days) = Injection date - date of preceding injection - 56 days
  - For participants transitioning from CAB+RPV Q4W in ATLAS on the Q8W arm, the Delay in

IP injection (days) will be calculated as:
Delay in IP Injection (days) = Injection date - date of preceding injection - 56 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 did not receive Week 48 injection (i.e. missing visit or withdrawal).

15.6.4. 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 2.1, March 2017, as specified in the protocol Appendix 11.2.

Potential QTc Interval Prolonging Events of Interest

Potential QTc Interval Prolonging Events of Interest 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

Adverse Events	
Ventricular flutter	
Ventricular tachyarrhythmia	

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 AI et al, 2012)

- Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [Levey et al, 2012] will be used by the central laboratory to provide an estimate of GFR, in mL/min per 1.73 m^2, as follows:

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

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 2.1, March 2017, as specified in the protocol of Appendix 11.2.

- Toxicities will be based on the Division of AIDS (DAIDS) grading system, Version 2.1, March 2.17, as specified in the protocol of Appendix 11.2
- Toxicity grades provided by the central laboratory do not distinguish between abnormally high or low criteria, when both are relevant for a 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.

Laboratory Parameters

Parameter	Below Midpoint for those ≥Grade 1	Above Midpoint for those ≥Grade 1
Fasted glucose	Hypoglycemia	Hyperglycemia
Sodium	Hyponatremia	Hypernatremia
Potassium	Hypokalemia	Hyperkalemia

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

Percentage change for lipids

The percentage change from baseline is calculated as:

$$\% \text{ change from baseline} = \frac{\text{value at Week 48 or 96} - \text{baseline value}}{\text{baseline value}} \times 100\%$$

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

Other Safety Endpoints

Corrected QT (QTc)

When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fridericia's

Other Safety Endpoints

(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.,

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

Extent of Exposure

- Exposure to CAB+RPV (oral lead-in or oral bridging) and CAB LA+RPV LA will be calculated from the IP eCRF pages.
- For Maintenance Phase:
  - Exposure to oral CAB+RPV (oral lead-in) = IP (oral lead-in) stop date - IP (oral lead-in) start date +1
  - Exposure to CAB LA + RPV LA = Number of IP injections received during maintenance phase (up to but not including injections administered at Week 100)
  - Overall exposure to IP:
    For participants on Q4W arm: min [Date of Latest Maintenance Phase Visit up to and including Week 100, max (Date of Last Injection + 35, Date of Last Dose of Oral CAB+RPV)] – min (Start Date for Oral lead-in CAB+RPV, Date of First Study Injection) + 1
    For participants on Q8W arm: min [Date of Latest Maintenance Phase Visit up to and including Week 100, max (Date of Last Injection + 63, Date of Last Dose of Oral CAB+RPV)] – min (Start Date for Oral lead-in CAB+RPV, Date of First Study Injection) + 1
- For Maintenance + Extension Phase
  - Exposure to CAB LA + RPV LA = Number of IP injections received during Maintenance Phase + Extension Phase
  - Overall Exposure to IP:
    For participants on Q4W arm: min [Date of Latest Visit, max (Date of Last Injection + 35, Date of Last Dose of Oral CAB+RPV)] – min (Start Date for Oral lead-in CAB+RPV, Date of First Study Injection) + 1
    For participants on Q8W arm: min [Date of Latest Visit, max (Date of Last Injection + 63, Date of Last Dose of Oral CAB+RPV)] – min (Start Date for Oral lead-in CAB+RPV, Date of First Study Injection) + 1
- Last Injection and/or Last Dose of Oral CAB+RPV are only applicable to those who permanently discontinued study treatment.

Other Safety Endpoints

- Duration of dosing in participant years will be calculated as the sum of participant duration of dosing in days (across all participants)/365.25
- Participants who were randomized 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 first injection". The injections of interest in adherence analysis are those after first injection. For participants requiring the oral CAB+RPV lead-in, the first injection is planned to be taken at Week 4B. For participants not requiring the oral CAB+RPV lead-in, the first injection is planned to be taken at Baseline/Day 1. 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 this participant 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

Columbia Suicide Severity Rating Scale (C-SSRS)

- Missing data will not have any imputation performed (Nilsson et al, 2013).

15.6.5. 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.

Pharmacokinetic Analyses

Plasma CAB and RPV Concentration-time Data

Plasma samples for determination of CAB and RPV concentration will be collected throughout the Maintenance Phase and at the withdrawal visit. Additional samples will be collected for storage during the Long-Term Follow-Up Phase.

Evaluable Concentration

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

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

- 20-28 hrs after last oral dose taken and properly administered last 3 oral doses for pre-dose sample at Week 4B for participants requiring oral lead-in
- ± 4 days for pre-dose sample at visits other than Week 4B, and for pre-dose samples at Week 4B for participants not requiring oral lead-in (e.g. participants transitioning from ATLAS Q4W and remain on Q4W arm in this study)
- 3-10 days post last injection for 1-week post injection visits;
- Samples impacted by dosing errors (wrong dose) or oral bridging will also be excluded

Timepoint	Evaluable Window	For Programming:
Pre-dose: WK4B for participants requiring oral lead-in	20-28 hrs after last oral dose taken and the last 3 oral doses administered properly	20 hrs ≤ Time since Last Oral Dose ≤ 28 hrs and the last 3 oral doses administered on the three consecutive days prior to WK4B.
Pre-dose at other visits, Pre-dose WK4B for participants not requiring oral lead-in	± 4 days	For Q4W arm, Day 1 pre-dose, and Week 8 for those transitioning from SOC (i.e. requiring oral lead-in) on Q8W arm: 24 days ≤ Days Since Last Injection ≤ 32 days For visits other than above on Q8W arm: 52 days ≤ Days Since Last Injection ≤ 60 days
1-WK-Post:	3-10 days post last injection	3 days ≤ Days Since Last Injection ≤ 10 days

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

Pharmacokinetic Analyses

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, the time of the first dose (not recorded in eCRF) is assumed to be 'after' the collection of pre-dose sample, unless medical monitor or Data querying informs otherwise.

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

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/WD	± 4 days	24 days ≤ Days Since Last Injection ≤ 32 days
LTFU MONTH 3	± 1 Weeks	77 days ≤ Days Since Last Injection ≤ 91 days
LTFU MONTH 6	± 2 Weeks	154 days ≤ Days Since Last Injection ≤ 182 days
LTFU MONTH 9	± 2 Weeks	238 days ≤ Days Since Last Injection ≤ 266 days
LTFU MONTH 12	± 2 Weeks	322 days ≤ Days Since Last Injection ≤ 350 days

15.6.6. Health Outcomes

HIVTSQs

Questionnaire (Questions 1-12 are scored

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

Total Treatment Satisfaction Score

- Total Treatment Satisfaction Score is computed with items 1-11. Items 1-11 are summed to produce a score with a possible range of CC to CC.
- Item 12 will not be included in Total Treatment Satisfaction Score. Instead, it will be treated as a stand-alone item only.
- Higher scores represent greater treatment satisfaction as compared to the past few weeks.
- A maximum of 5 items can be missing, which can be imputed to reflect the mean of the completed item scores. If 6 or more items are missing, then the treatment satisfaction scale score should not be computed and instead be imputed using LOCF.

Individual Item Scores

- Items are rated as C (CCI , etc.) to C (CCI , CCI , etc.).
- Higher scores represent greater satisfaction with each aspect of treatment
  - For individual item scores outputs, missing scores will not be computed (according to Page 7 of the [HIVTSQ User Guidelines, 2016]) and instead be imputed using LOCF.

HIVTSQc

Questionnaire (Questions 1-12 are scored CC to C)

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Total Treatment Satisfaction Score (change)

- Total Treatment Satisfaction Score is computed with items 1-11. Items 1-11 are summed to produce a score with a possible range of CCI to CCI
- Item 12 will be computed as an individual item only.
- The higher the score, the greater the improvement in satisfaction with treatment; the lower the score, the greater the deterioration in satisfaction with treatment. A score of C represents CCI CCI .
- A maximum of 5 items can be missing, the missing scores will be imputed with the mean of the completed item scores. If 6 or more items are missing, then the overall treatment satisfaction scale score should not be computed and will remain missing.

Individual Treatment Satisfaction Change Item Scores

- Items are rated as CCI (CCI , etc.) to CCI (‘CCI , etc.).
- The higher the score, the greater the improvement in satisfaction with each aspect of treatment and the lower the score, the greater the deterioration in satisfaction with each aspect of treatment.

Questionnaire Version

- Three versions of the HIVTSQc questionnaire are available with the questions the same and only the overhead text is different.
  - Q4W ATLAS to Q4W ATLAS-2M: for participants who randomized to Q4W arm in ATLAS and then randomized to Q4W arm in ATLAS-2M
  - Q4W ATLAS to Q8W ATLAS-2M: for participants who randomized to Q4W arm in ATLAS and then randomized to Q8W arm in ATLAS-2M
  - SOC to Q4W or Q8W ATLAS-2M: for participants who either were randomized to SOC arm in ATLAS or did not participate in ATLAS
- If a participant takes a wrong version of the questionnaire, the data collected from the wrong version will be considered invalid and will not be included in the summary.

PIN

Questionnaire (Each question is scored CCI)

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Dimension Score (Chevat et al, 2008)

- Domains and Clusters
  - CCI: items CCI
  - CCI: items CCI
  - CCI: items CCI
  - CCI: items CCI
- 5 items not included in any of these domains and maintained as individual items (items CCI) (CCI)
- No overall score is calculated per the guidance
- The score of a domain is calculated as the mean of all items with the domain. Higher scores represent worse perception of injection.
- A maximum of <50% items can be missing within a domain, which can be imputed to reflect the mean of the completed item scores within the domain. Thus, if the number of missing items is ≥3 (CCI), ≥2 (CCI), ≥1 (CCI), then the total score for the domain should not be computed and instead be imputed using LOCF (Section 15.7.2.2)

Individual Item Scores

- Items are rated on a 5-point scale, ranging from CCI, etc.) to CCI (CCI, etc.).
- Lower scores represent worse perception of injection
- For individual item scores outputs, missing scores will not be computed and instead be imputed using LOCF (Section 15.7.2.2).

HAT-QoL (Holmes, 1999)

Questionnaire (Questions 1-14 are scored CCI to CCI

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Life satisfaction, HIV medications, disclosure worries

- The ratings for Items (a, b, c, d, e) will be recoded as below for analysis:

  Response option Life Satisfaction Medication/disclosure worries

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- A maximum of 50% question items can be missing within a domain, which can be computed and replaced with the mean of the completed item scores within the domain. Thus, if there are more than 1 item missing for Life Satisfaction, and more than 2 items missing for Medication/disclosure worries, then the total score for the domain should not be computed and instead be imputed using LOCF (Section 15.7.2.2). A computed score for missing value will be added to calculate a total score for the domain. Total score for each of the three domains will be calculated and will be denoted as 'LISAT' for life satisfaction, 'MEDWO' for medication worries, and 'DISWO' for disclosure worries.
- Transform each dimension's total imputed value score to the 0-100 scale using the following formulae:

  Life satisfaction: CCI

  Medication worries: CCI

  Disclosure worries: CCI

  The higher the score, the greater satisfaction to life and the less worry. The transformed dimension score for each domain will be summarized and analysed.

Individual Item Scores

- For individual item scores outputs, missing scores will not be computed and instead be imputed using LOCF (Section 15.7.2.2).

ACCEPT (Acceptance/General Dimension) (Gilet H et al, 2014)

Questionnaire (Questions 1-3 constitute to Acceptance/General Dimension)

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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.

- Proportion of participants with individual item scores will be calculated.

Individual Item Scores

- Items are rated as C CI(CCI) to C CI(CCI). and 'C with 'CCI '.
- Acceptance/General dimension score is calculated only if at least 2 items in the dimension are completed
- Items will be recoded to score as follows:

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

- The total score of the dimension is calculated as the mean of the recoded items of the dimension and then linearly transformed to be on a scale from C CI to CCI score, as below:

  Total Score = CCI

- For individual item scores outputs, missing scores will not be computed and instead be imputed using LOCF (Section 15.7.2.2).

Preference

Questionnaire

1. Based on your experience which HIV treatment do you prefer?

□ Injectable Long-Acting HIV Treatment every 4 weeks
□ Injectable Long-Acting HIV Treatment every 8 weeks (only select this answer if you received the 8-week injectable regimen of CAB LA + RPV LA during study)
□ Oral daily HIV Treatment
□ No preference

If you selected no preference, skip questions 2 and 3.
If you selected any other response, please continue and complete all questions.

2. What is the main practical attribute of this HIV therapy supporting your preference?

□ Mode of administration
□ Frequency of administration
□ Time required for administration
□ Scheduling visits
□ Storing medications
□ Impact of side effects

□ Other, please specify 3. What is the main benefit related to this HIV therapy supporting your preference? □ More convenient, easier to integrate into one's daily life □ Less stressful □ Less stigma □ Easier to take the drug exactly as prescribed □ More efficacious □ Other, please specify
Questionnaire Version
• Two versions of questionnaire are available. The questions in each version of the questionnaire are the same and only the overhead text is different. o ATLAS (from Q4W ATLAS): for participants randomized to Q4W arm in ATLAS. o ATLAS-2M (from SOC ATLAS or out): for participants who either were randomized to SOC arm in ATLAS or did not participate in ATLAS.
Data Handling
• Any missing values will remain missing (i.e. no imputation).
Reasons for Continuation/Switch
Questionnaires
• Reasons for Continuation questionnaire is collected for participants who were randomized to Q4W arm in ATLAS. • Reason for Switch questionnaire is collected for participants who either were randomized to SOC arm in ATLAS or did not participate in ATLAS.
Data Handling
• If a participant takes a wrong questionnaire, for example, the participant randomized to SOC arm in ATLAS took Reasons for Continuation questionnaire, the data collected from this wrong version will be considered invalid and will not be included in the summary. • If the questionnaire is taken beyond ± 2 weeks window from maintenance phase treatment start date (i.e. Study Day < -14 or Study Day > 14) will be consider not evaluable and will not be included in the summary. • Any missing values will remain missing (i.e. no imputation).

15.6.7. Virology

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

Representation of Amino Acid Changes

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

Resistance Associated Mutations

- Known INI mutations associated with the development of resistance to BIC, 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/M*, 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 18Jul2018) and accessed on 06Oct2018.
- 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 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 AM et al 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 et al. 2017]

Phenotype

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.

Phenotypic susceptibilities will be categorised according to FC as shown in tables below (based on Monogram PhenoSense assay). Clinical cutoffs (where available) or biological cutoffs by PhenoSense will be used to define the phenotypic susceptibility of background treatment by Monogram.

Replication capacity is generated as part of standard phenotypic assays.

PhenoSense Algorithm

Drug	Abbreviation	Class	PhenoSense cutoff
Abacavir	ABC	NRTI	(4.5 – 6.5)[a]
Lamivudine	3TC	NRTI	3.5 [a]
Didanosine	ddI	NRTI	(1.3 – 2.2) [a]
Stavudine	d4T	NRTI	1.7 [a]
Zidovudine	AZT (ZDV)	NRTI	1.9
Emtricitabine	FTC	NRTI	3.5
Tenofovir	TDF (TAF)	NRTI	(1.4 – 4) [a]
Delavirdine	DLV	NNRTI	6.2
Efavirenz	EFV	NNRTI	3
Nevirapine	NVP	NNRTI	4.5
Etravirine	ETR	NNRTI	(2.9-10) [a]
Rilpivirine	RPV	NNRTI	2.0
Fosamprenavir/r	FPV/r	PI	(4-11) [a]
Atazanavir	ATV	PI	2.2[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]
Bictegravir	BIC	INI	(2.5- 10)

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

Phenotypic Susceptibility

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 biological cutoff	resistant
≤ clinical lower cutoff or biological cutoff	sensitive

Partial Sensitivity

Fold Change	Interpretation
> clinical higher cutoff	resistant
≤ 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. Net assessment susceptibility will be reported with the categories of 'resistant', 'partially sensitive', and 'sensitive' as what will be performed for phenotypic susceptibility. Genotypic susceptibility will be reported with the categories of 'resistant', 'resistance possible' and 'sensitive'. Genotypic and Net assessment susceptibility will be assessed at time of CVF using plasma sample, Genotypic susceptibility may be assessed at baseline using PBMC.

15.7. Appendix 7: Reporting Standards for Missing Data

15.7.1. Premature Withdrawals

Element	Reporting Detail

General	• Participant study completion (i.e. as specified in the protocol) was defined as
	  ○ Randomly assigned to either treatment group, completed the randomized Maintenance Phase including Week 100 and did not enter the Extension Phase;
	  ○ Randomly assigned to either treatment group, completed the randomized Maintenance Phase including Week 100, and entered and completed the Extension Phase (defined as remaining on study until commercial supplies of CAB LA + RPV LA Q4W or Q8W regimen become locally available or development of CAB LA + RPV LA is terminated).
	
	Participants who withdraw from CAB LA + RPV LA and go into the LTFU Phase, and participants who withdraw from oral lead-in will be considered to have prematurely withdrawn from the study treatment.
	
	In addition to the 52-week Follow-Up phase required for participants who receive one or more injections with CAB LA or RPV LA, an in-clinic Follow-Up visit will be conducted approximately 4 weeks after the last dose of study medication for participants who withdraw during the oral lead-in period with ongoing AEs, and serious adverse events (SAEs) and also any laboratory abnormalities that are considered to be AEs or potentially harmful to the participant, at the last on-study visit. Assessments at the Follow-up visit should reflect any ongoing complaints (e.g., blood draws to follow a laboratory abnormality). Follow-Up visits are not required for successful completion of the study.
	
	• Withdrawn participants were not replaced in the study.
	• All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.
	• Withdrawal visits will be slotted as per Appendix 3: Assessment Windows or will be summarised as withdrawal visits.

15.7.2. Handling of Missing Data

Element	Reporting Detail

General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument:
	  ○ These data will be indicated by the use of a “blank” in participant listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table.
	  ○ Answers such as “Not applicable” and “Not evaluable” are not considered to be missing data and should be displayed as such.

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

15.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant 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: ○ Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 4: Study Phases and Treatment State. ○ Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.
ART/Non-ART Medications or Medical History	• Partial dates recorded in the eCRF will be imputed using the following convention: ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month. ○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. If medications recorded in the eCRF as prior (e.g. recorded in prior ART or prior ATLAS ART forms, taken prior to study), the earlier date of the imputed and the day prior to the maintenance phase treatment start date will be used, i.e. min (imputed stop date, maintenance phase treatment start date - 1). • For medications with completely missing start date, they will be considered started prior to the maintenance phase treatment start date. • For medications with completely missing stop date, they will be considered ongoing unless recorded in eCRF as prior (e.g. recorded in prior ART or prior ATLAS ART forms, taken prior to study). • For ART booster medications, the start and stop dates are not recorded in the database (i.e. missing), the dates will be imputed to be the same as the dates of their parent medications. • The recorded partial or missing date will be displayed in listings.
Health outcomes	• For the health outcomes questionnaire data, please refer to Section12. • For the summary of individual item scores outputs, missing scores will not be computed.

15.7.2.2. 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 c/mL' (or ''HIV-1 RNA ≥ 200 c/mL') or 'No Virologic Data at Week X'; Appendix 9: Snapshot Algorithm Details for full details
LOCF	• In the LOCF dataset, missing values will be carried forward from the previous, non-missing available on-treatment assessment. If the baseline value is missing any missing values until the first non-missing value will remain missing.
Lipid LOCF	**Baseline for Lipids LOCF Analyses**: • Last evaluable lipids assessment up to and including the start of IP, where 'evaluable' is defined as: Lipid modifying agents not taken within 12 weeks of the date of assessment and Lipids are collected in a fasting state. Participants with unevaluable Baseline for Lipids (as defined above) will be excluded from this dataset. **During the Maintenance**: • If participants initiate serum lipid-lowering agents during the maintenance, then the last available fasted on-treatment lipid values prior to the initiation will be used in place of future, observed on-treatment values. • Imputation at visits with observed on-treatment values will continue even if the participant discontinues the lipid-lowering agent. Missing assessments will not be imputed **Analyses Evaluated with Lipid LOCF Dataset:** This dataset will be used to summarize fasting lipids parameters in the following displays: Summary of Fasting TC/HDL ratio Change from Baseline Summary of Fasting Lipids Percentage Changes from Baseline All other displays of lipids (e.g. toxicity tables and NCEP tables) will use observed fasting data, without LOCF imputation.

15.8. Appendix 8: Values of Potential Clinical Importance

ECG values of potential clinical importance are defined as QTc > 500 msec or increase from baseline in QTc ≥ 60 msec.

15.9. Appendix 9: Snapshot Algorithm Details

Detailed Algorithm Steps

- Consider an analysis visit window for Week X as defined in Table 10.
- The HIV-1 RNA threshold of 50, 200 c/mL will be analysed, respectively, in this study
- The analysis window 'Week 48' and HIV-1 RNA threshold of '50 c/mL' are used for the purpose of illustration. A participant's Snapshot response and reason at Week 48 are categorized as below.

  - HIV-1 RNA < **50** c/mL
  - HIV-1 RNA ≥ **50** c/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 permanent change in ART are not permitted in this protocol, all such participants who permanently change ART will be considered 'HIV-1 RNA ≥ 50 c/mL' if the permanent change in ART is made prior to an analysis timepoint. Participants with protocol permitted oral bridging treatment or a temporary change in ART prior to an analysis timepoint (e.g. participant took the ART different from study treatment during oral lead-in by mistake for a short period and then went back to the study treatment) will not be considered 'HIV-1 RNA ≥ 50 c/mL' due to 'change in ART'.

- The steps in determining response and reasons are indicated in the table below, in the order stated:

Detailed steps

Please note that the following scenarios will NOT be penalized Per Snapshot algorithm (i.e. please exclude 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	HIV-1 RNA ≥ 50	Change in background therapy
2. If permitted change[a] in background therapy prior to Week 48 AND the latest on-treatment VL prior to/on the date of change is ≥ 50 c/mL (NA to this study)	HIV-1 RNA ≥ 50	Change in 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	HIV-1 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	HIV-1 RNA < 50	
• No VL during Week 48 prior to/on the date of change	HIV-1 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	HIV-1 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	HIV-1 RNA ≥ 50	Data in window not below 50
5. If none of the above conditions met		
5.1 On-treatment VL available during Week 48		
• Last on-treatment VL during Week 48 ≥ 50 c/mL	HIV-1 RNA ≥ 50	Data in window not below 50
• Last on-treatment VL during Week 48 < 50 c/mL	HIV-1 RNA < 50	
5.2 No on-treatment VL during Week 48		
5.2.1 If participants still on study, i.e. a participant has not permanently discontinued the study treatment yet, or if a participant permanently discontinued the study treatment and the upper bound of analysis snapshot window is prior to the following date: Q8W arm: Min[max(Date of last injection + 63, Date of Last Dose of Oral CAB+RPV + 1), Withdrawal Date] Q4W arm: Min[max(Date of last injection + 35, Date of Last Dose of	No virologic data at Week 48 Window	On study but missing data in window

Oral CAB+RPV + 1), Withdrawal Date] , where 'Withdrawal Date' refers to the date the participant failed to complete per corresponding conclusion form.		
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 etc, 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 etc, 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	HIV-1 RNA ≥ 50	Disc. for lack of efficacy
• Last on-treatment VL ≥ 50 c/mL AND withdrawal due to all other non-safety related reasons	HIV-1 RNA ≥ 50	Disc. for other reason while not below 50

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

Examples from FDA guidance

Data in Window

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

- HIV-1 RNA = 580 c/mL at Day 336, HIV-1 RNA below 50 c/mL on Day 350. This should be categorized as HIV-1 RNA below 50 c/mL.

No Data in Window

Discontinued study due to Adverse Event or Death:

- Any patient who discontinues because of an AE or death before the window should be classified as *Discontinued due to AE or Death* (as appropriate), regardless of the HIV-1 RNA result, even if the HIV-1 RNA is below 50 c/mL at the time of discontinuation.
- However, if a patient has an HIV-1 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-1 RNA below 50 c/mL at Day 336 and discontinues because of AE or even dies on Day 360 — this person is categorized as having HIV-1 RNA below 50 c/mL.

b. HIV-1 RNA is 552 c/mL on Day 336 and the patient discontinues on Day 360, the patient is categorized as having HIV-1 RNA ≥ 50 c/mL.

Discontinued for Other Reasons:

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

On study but missing data in window:

- If there are no data during Days 294 to 377, but there is an HIV-1 RNA below 50 c/mL on Day 380, this patient should be considered *On Study but Missing Data in Window.*
- If there are no data during Days 294 to 377, but there is an HIV-1 RNA equal to or above 50 c/mL on Day 280, this patient also should be classified as *On Study but Missing Data in Window.*

15.10. Appendix 10: 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 AVAL=Study Day of SVF* *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 Note: primary reason and/or standardized subreason for discontinuation based on Maintenance Conclusion form in the eCRF. 'Protocol Defined Safety Stopping Criteria' includes GSK defined liver chemistry stopping criteria, renal toxicity criteria and QTc withdrawal criteria. Treatment Related AE' is defined as participants who have primary reason for withdrawal =AE and who have at least one AE considered drug related and leading to withdrawal/permanent discontinuation of investigational product.	CNSR=0	EVNTDESC= terms in italic, respectively. For Q4W arm: AVAL= min [Study Day of Maintenance Phase Discontinuation, max(Study Day of Last Injection + 35, Study Day of Last Dose of Oral CAB+RPV + 1)] For Q8W arm: AVAL= min [Study Day of Maintenance Phase Discontinuation, max(Study Day of Last Injection + 63, Study Day of Last Dose of Oral CAB/RPV + 1)] 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' AVAL will be defined as the same as above 2
4. Participant who did not have premature withdrawal from	CNSR=1	EVNTDESC='Censored due to data cutoff for analysis'

Programming Instructions for the Kaplan-Meier analysis of treatment-related discontinuation equals failure (TRDF)		
Condition	**Censor Status**	**Event Description/AVAL**
the Maintenance Phase		AVAL = Study Day of last on-treatment date during the maintenance phase, which is defined as follows: For Q4W arm: min [Study Day of Nominal Week 100 Visit, Study Day of LTFU ART Start Date, Study Day of Last Contact Date at time of analysis, max(Study Day of Last Injection + 35, Study Day of Last Dose of Oral CAB+RPV + 1)] For Q8W arm min [Study Day of Nominal Week 100 Visit, Study Day of LTFU ART Start Date, Study Day of Last Contact Date at time of analysis, max(Study Day of Last Q8W IM Dose + 63, Study Day of Last Dose of Oral CAB+RPV + 1)]

Note that last injection and last dose of oral CAB+RPV mentioned in table above are only applied to participants who permanently discontinued from the study treatment. The similar approach will be used to derive for Kaplan-Meier analysis of efficacy-related discontinuation equals failure (ERDF), except that the reason of withdrawal in Condition 2 will be restricted to 'Lack of Efficacy'.

15.11. Appendix 11: Identification of Adverse Events of Special Interest

The adverse events of special interest are identified based on MedDRA coded values and/or AE data available in the study database. The system organ classes (SOCs), preferred terms (PTs) or codes, Standardised MedDRA Queries (SMQs), High Level Group Terms (HLGTs), and High Level Terms (HLTs) below are from MedDRA 21.1. SMQs use narrow terms unless otherwise specified. In case there is a change to the version of MedDRA at time of reporting, the coded values based on the MedDRA version at the time of reporting will be used. The additional events may also be added based on the blinded review of AE data collected on study prior to the database freeze.

1. Hepatic Safety Profile: Assessment of risk of hepatoxicity

Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions (SMQ)

PT	PT Code
Acquired hepatocerebral degeneration	10080860
Acute hepatic failure	10000804
Acute on chronic liver failure	10077305
Acute yellow liver atrophy	10070815
Ascites	10003445
Asterixis	10003547
Bacterascites	10068547
Biliary cirrhosis	10004659
Biliary fibrosis	10004664
Cholestatic liver injury	10067969
Chronic hepatic failure	10057573
Coma hepatic	10010075
Cryptogenic cirrhosis	10063075
Diabetic hepatopathy	10071265
Drug-induced liver injury	10072268
Duodenal varices	10051010
Gallbladder varices	10072319
Gastric variceal injection	10076237
Gastric variceal ligation	10076238
Gastric varices	10051012
Gastric varices haemorrhage	10057572
Hepatectomy	10061997
Hepatic atrophy	10019637
Hepatic calcification	10065274
Hepatic cirrhosis	10019641
Hepatic encephalopathy	10019660
Hepatic encephalopathy prophylaxis	10066599

PT	PT Code
Hepatic failure	10019663
Hepatic fibrosis	10019668
Hepatic hydrothorax	10067365
Hepatic infiltration eosinophilic	10064668
Hepatic lesion	10061998
Hepatic necrosis	10019692
Hepatic steato-fibrosis	10077215
Hepatic steatosis	10019708
Hepatitis fulminant	10019772
Hepatobiliary disease	10062000
Hepatocellular foamy cell syndrome	10053244
Hepatocellular injury	10019837
Hepatopulmonary syndrome	10052274
Hepatorenal failure	10019845
Hepatorenal syndrome	10019846
Hepatotoxicity	10019851
Intestinal varices	10071502
Intestinal varices haemorrhage	10078058
Liver and small intestine transplant	10052280
Liver dialysis	10076640
Liver disorder	10024670
Liver injury	10067125
Liver operation	10062040
Liver transplant	10024714
Lupoid hepatic cirrhosis	10025129
Minimal hepatic encephalopathy	10076204
Mixed liver injury	10066758
Nodular regenerative hyperplasia	10051081
Non-alcoholic fatty liver	10029530
Non-alcoholic steatohepatitis	10053219
Non-cirrhotic portal hypertension	10077259
Oedema due to hepatic disease	10049631
Oesophageal varices haemorrhage	10030210
Peripancreatic varices	10073215
Portal fibrosis	10074726
Portal hypertension	10036200
Portal hypertensive colopathy	10079446
Portal hypertensive enteropathy	10068923
Portal hypertensive gastropathy	10050897

PT	PT Code
Portal vein cavernous transformation	10073979
Portal vein dilatation	10073209
Portopulmonary hypertension	10067281
Primary biliary cholangitis	10080429
Regenerative siderotic hepatic nodule	10080679
Renal and liver transplant	10052279
Retrograde portal vein flow	10067338
Reye's syndrome	10039012
Reynold's syndrome	10070953
Splenic varices	10067823
Splenic varices haemorrhage	10068662
Steatohepatitis	10076331
Subacute hepatic failure	10056956
Varices oesophageal	10056091
Varicose veins of abdominal wall	10072284
White nipple sign	10078438

Hepatitis, non-infectious (SMQ)

PT	PT Code
Acute graft versus host disease in liver	10066263
Allergic hepatitis	10071198
Alloimmune hepatitis	10080576
Autoimmune hepatitis	10003827
Chronic graft versus host disease in liver	10072160
Chronic hepatitis	10008909
Graft versus host disease in liver	10064676
Hepatitis	10019717
Hepatitis acute	10019727
Hepatitis cholestatic	10019754
Hepatitis chronic active	10019755
Hepatitis chronic persistent	10019759
Hepatitis fulminant	10019772
Hepatitis toxic	10019795
Immune-mediated hepatitis	10078962
Ischaemic hepatitis	10023025
Lupus hepatitis	10067737
Non-alcoholic steatohepatitis	10053219
Radiation hepatitis	10051015
Steatohepatitis	10076331

2. Hypersensitivity Reactions (HSR)

Drug reaction with eosinophilia and systemic symptoms syndrome (SMQ)

PT	PT Code
Drug reaction with eosinophilia and systemic symptoms	10073508
Pseudolymphoma	10037127

PTs (Selective)

PT	PT Code
Drug hypersensitivity	10013700
Hypersensitivity	10020751
Type IV Hypersensitivity reaction	10053613
Eosinophillia	10014950
Eye swelling	10015967
Eyelid oedema	10015993
Lip swelling	10024570
Angioedema	10002424
Circumoral oedema	10052250
Face oedema	10016029
Idiopathic angioedema	10073257
Lip oedema	10024558
Mouth swelling	10075203
Oedema mouth	10030110
Periorbital oedema	10034545
Swelling face	10042682
Periorbital swelling	10056647
Swelling of eyelid	10042690

3. Rash

Severe cutaneous adverse reactions (SMQ)

PT	PT Code
Acute generalised exanthematous pustulosis	10048799
Cutaneous vasculitis	10011686
Dermatitis bullous	10012441
Dermatitis exfoliative	10012455
Dermatitis exfoliative generalised	10012456
Drug reaction with eosinophilia and systemic symptoms	10073508

PT	PT Code
Epidermal necrosis	10059284
Erythema multiforme	10015218
Exfoliative rash	10064579
Oculomucocutaneous syndrome	10030081
Skin necrosis	10040893
Stevens-Johnson syndrome	10042033
Toxic epidermal necrolysis	10044223
Toxic skin eruption	10057970

PTs (Selective), Grade 3 and higher

PT	PT Code
Eyelid rash	10074620
Genital rash	10018175
Mucocutaneous rash	10056671
Nodular rash	10075807
Perineal rash	10075364
Rash	10037844
Rash erythematous	10037855
Rash generalised	10037858
Rash macular	10037867
Rash maculo-papular	10037868
Rash maculovesicular	10050004
Rash morbilliform	10037870
Rash papular	10037876
Rash rubelliform	10057984
Rash scarlatiniform	10037890
Rash vesicular	10037898
Rash pruritic	10037884
Rash follicular	10037857
Rash pustular	10037888
Drug eruption	10013687

4. Prolongation of the Corrected QT Interval of the ECG in Supratherapeutic Doses

Torsade de pointes/QT prolongation (SMQ)

PT	PT Code
Electrocardiogram QT interval abnormal	10063748

PT	PT Code
Electrocardiogram QT prolonged	10014387
Long QT syndrome	10024803
Long QT syndrome congenital	10057926
Torsade de pointes	10044066
Ventricular tachycardia	10047302

PTs (Selective)

PT	PT Code
Electrocardiogram repolarisation abnormality	10052464

5. Suicidal Ideation/Behaviour

Suicide/self-injury (SMQ)

PT	PT Code
Assisted suicide	10079105
Columbia suicide severity rating scale abnormal	10075616
Completed suicide	10010144
Depression suicidal	10012397
Intentional overdose	10022523
Intentional self-injury	10022524
Poisoning deliberate	10036000
Self-injurious ideation	10051154
Suicidal behaviour	10065604
Suicidal ideation	10042458
Suicide attempt	10042464
Suicide threat	10077417
Suspected suicide attempt	10081704

6. Depression

Depression (excl suicide and self injury) (SMQ)

PT	PT Code
Activation syndrome	10066817
Adjustment disorder with depressed mood	10001297
Adjustment disorder with mixed anxiety and depressed mood	10001299
Agitated depression	10001496
Anhedonia	10002511

PT	PT Code
Antidepressant therapy	10054976
Childhood depression	10068631
Decreased interest	10011971
Depressed mood	10012374
Depression	10012378
Depression postoperative	10012390
Depressive symptom	10054089
Dysphoria	10013954
Electroconvulsive therapy	10014404
Feeling guilty	10049708
Feeling of despair	10016344
Feelings of worthlessness	10016374
Helplessness	10077169
Major depression	10057840
Menopausal depression	10067371
Mixed anxiety and depressive disorder	10080836
Perinatal depression	10078366
Persistent depressive disorder	10077804
Post stroke depression	10070606
Postictal depression	10071324

7. Bipolar Disorder

HLGT Manic and Bipolar mood disorders and disturbances

PT	PT Code
Bipolar I disorder	10004939
Bipolar II disorder	10004940
Bipolar disorder	10057667
Cyclothymic disorder	10011724
Hypomania	10021030
Mania	10026749

8. Psychosis

Psychosis and psychotic disorders (SMQ)

PT	PT Code
Acute psychosis	10001022
Alcoholic psychosis	10001632

PT	PT Code
Alice in wonderland syndrome	10001666
Brief psychotic disorder with marked stressors	10048549
Brief psychotic disorder without marked stressors	10056395
Brief psychotic disorder, with postpartum onset	10006362
Charles Bonnet syndrome	10063354
Childhood psychosis	10061040
Clang associations	10009232
Cotard's syndrome	10059591
Delusion	10012239
Delusion of grandeur	10012241
Delusion of reference	10012244
Delusion of replacement	10012245
Delusional disorder, erotomanic type	10012249
Delusional disorder, grandiose type	10012250
Delusional disorder, jealous type	10012251
Delusional disorder, mixed type	10012252
Delusional disorder, persecutory type	10053195
Delusional disorder, somatic type	10012254
Delusional disorder, unspecified type	10012255
Delusional perception	10012258
Dementia of the Alzheimer's type, with delusions	10012295
Depressive delusion	10063033
Derailment	10012411
Epileptic psychosis	10059232
Erotomanic delusion	10015134
Flight of ideas	10016777
Hallucination	10019063
Hallucination, auditory	10019070
Hallucination, gustatory	10019071
Hallucination, olfactory	10019072
Hallucination, synaesthetic	10062824
Hallucination, tactile	10019074
Hallucination, visual	10019075
Hallucinations, mixed	10019079
Hypnagogic hallucination	10020927
Hypnopompic hallucination	10020928
Hysterical psychosis	10062645
Ideas of reference	10021212
Illusion	10021403

PT	PT Code
Jealous delusion	10023164
Loose associations	10024825
Mixed delusion	10076429
Neologism	10028916
Neuroleptic-induced deficit syndrome	10075295
Paranoia	10033864
Paranoid personality disorder	10033869
Parkinson's disease psychosis	10074835
Paroxysmal perceptual alteration	10063117
Persecutory delusion	10034702
Postictal psychosis	10070669
Post-injection delirium sedation syndrome	10072851
Posturing	10036437
Psychosis postoperative	10065617
Psychotic behaviour	10037249
Psychotic disorder	10061920
Psychotic disorder due to a general medical condition	10061921
Reactive psychosis	10053632
Rebound psychosis	10074833
Schizoaffective disorder	10039621
Schizoaffective disorder bipolar type	10068889
Schizoaffective disorder depressive type	10068890
Schizophrenia	10039626
Schizophreniform disorder	10039647
Schizotypal personality disorder	10039651
Senile psychosis	10039987
Shared psychotic disorder	10040535
Somatic delusion	10041317
Somatic hallucination	10062684
Substance-induced psychotic disorder	10072388
Tangentiality	10043114
Thought blocking	10043495
Thought broadcasting	10052214
Thought insertion	10043496
Thought withdrawal	10043497
Transient psychosis	10056326
Waxy flexibility	10047853

9. Mood Disorders

HLGT Mood disorders and disturbances NEC, Psychiatric disorders SOC

PT	PT Code
Crying	10011469
Mood swings	10027951
Boredom	10048909
Mood altered	10027940
Apathy	10002942
Affective ambivalence	10077173
Emotional poverty	10014557
Euphoric mood	10015535
Premenstrual dysphoric disorder	10051537
Alexithymia	10077719
Laziness	10051602
Blunted affect	10005885
Constricted affect	10010778
Affect lability	10054196
Anger	10002368
Affective disorder	10001443
Lethargy	10024264
Listless	10024642
Inappropriate affect	10021588
Dysphoria	10013954
Mood disorder due to a general medical condition	10027944
Morose	10027977
Screaming	10039740
Steroid withdrawal syndrome	10042028
Emotional disorder	10014551
Irritability	10022998
Moaning	10027783
Premenstrual syndrome	10036618
Neuroleptic-induced deficit syndrome	10075295
Substance-induced mood disorder	10072387
Flat affect	10016759
Diencephalic syndrome of infancy	10012774
Emotional distress	10049119
Frustration tolerance decreased	10077753
Seasonal affective disorder	10039775

10. Anxiety

HLGT Anxiety disorders and symptoms

PT	PT Code
Acrophobia	10000605
Activation syndrome	10066817
Acute stress disorder	10001084
Aerophobia	10080300
Agitation	10001497
Agitation neonatal	10001500
Agitation postoperative	10049989
Agoraphobia	10001502
Akathisia	10001540
Algophobia	10078056
Animal phobia	10002518
Anniversary reaction	10074066
Anticipatory anxiety	10002758
Anxiety	10002855
Anxiety disorder	10057666
Anxiety disorder due to a general medical condition	10002859
Arachnophobia	10051408
Astraphobia	10078372
Autophobia	10071070
Body dysmorphic disorder	10052793
Burnout syndrome	10065369
Claustrophobia	10009244
Compulsions	10010219
Compulsive cheek biting	10076510
Compulsive handwashing	10071263
Compulsive hoarding	10068007
Compulsive lip biting	10066241
Compulsive shopping	10067948
Dermatillomania	10065701
Dysmorphophobia	10049096
Emetophobia	10070637
Fear	10016275
Fear of animals	10016276
Fear of closed spaces	10016277
Fear of crowded places	10050365
Fear of death	10066392

PT	PT Code
Fear of disease	10016278
Fear of eating	10050366
Fear of falling	10048744
Fear of injection	10073753
Fear of open spaces	10016279
Fear of pregnancy	10067035
Fear of weight gain	10016280
Fear-related avoidance of activities	10080136
Generalised anxiety disorder	10018075
Glossophobia	10080077
Haemophobia	10073458
Haphephobia	10067580
Hydrophobia	10053317
Hyperarousal	10080831
Immunisation anxiety related reaction	10075205
Kinesiophobia	10078430
Limited symptom panic attack	10024511
Mysophobia	10078769
Nail picking	10066779
Nervousness	10029216
Neurosis	10029333
Noctiphobia	10057946
Nocturnal fear	10057948
Nosophobia	10063546
Obsessive need for symmetry	10077179
Obsessive rumination	10056264
Obsessive thoughts	10029897
Obsessive-compulsive disorder	10029898
Obsessive-compulsive symptom	10077894
Ochlophobia	10050095
Osmophobia	10060765
Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection	10072147
Panic attack	10033664
Panic disorder	10033666
Panic reaction	10033670
Paruresis	10069024
Performance fear	10034432
Phagophobia	10050096
Pharmacophobia	10069423

PT	PT Code
Phobia	10034912
Phobia of driving	10056676
Phobia of exams	10034913
Phobic avoidance	10034918
Phonophobia	10054956
Photaugiaphobia	10064420
Post-traumatic stress disorder	10036316
Postpartum neurosis	10036419
Postpartum stress disorder	10056394
Procedural anxiety	10075204
Pseudoangina	10056610
Selective mutism	10039917
Separation anxiety disorder	10040045
Sitophobia	10080170
Social anxiety disorder	10041242
Social fear	10041247
Stress	10042209
Tension	10043268
Terminal agitation	10077416
Thanatophobia	10064723
Thermophobia	10075147
Trichotemnomania	10072752
Trichotillomania	10044629

11. Sleep Disorders

HLGT Sleep Disorders and Disturbances

PT	PT Code
Behavioural insomnia of childhood	10072072
Hyposomnia	10067530
Initial insomnia	10022035
Insomnia	10022437
Middle insomnia	10027590
Terminal insomnia	10068932
Breathing-related sleep disorder	10006344
Dyssomnia	10061827
Hypersomnia	10020765
Periodic limb movement disorder	10064600
Pickwickian syndrome	10035004

PT	PT Code
Poor quality sleep	10062519
Sleep apnoea syndrome	10040979
Somnolence	10041349
Somnolence neonatal	10041350
Stupor	10042264
Upper airway resistance syndrome	10063968
Cataplexy	10007737
Hypnagogic hallucination	10020927
Hypnopompic hallucination	10020928
Narcolepsy	10028713
Sleep attacks	10040981
Sleep paralysis	10041002
Abnormal dreams	10000125
Abnormal sleep-related event	10061613
Confusional arousal	10067494
Exploding head syndrome	10080684
Loss of dreaming	10065085
Nightmare	10029412
Parasomnia	10061910
Rapid eye movement sleep behaviour disorder	10077299
Rapid eye movements sleep abnormal	10037841
Sleep inertia	10067493
Sleep sex	10067492
Sleep talking	10041009
Sleep terror	10041010
Sleep-related eating disorder	10067315
Somnambulism	10041347
Hypersomnia related to another mental condition	10020767
Hypersomnia-bulimia syndrome	10053712
Insomnia related to another mental condition	10022443
Sleep disorder	10040984
Sleep disorder due to a general medical condition	10063910
Sleep disorder due to general medical condition, hypersomnia type	10040985
Sleep disorder due to general medical condition, insomnia type	10040986
Sleep disorder due to general medical condition, mixed type	10040987
Sleep disorder due to general medical condition, parasomnia type	10040988
Sopor	10058709

PT	PT Code
Advanced sleep phase	10001423
Circadian rhythm sleep disorder	10009191
Delayed sleep phase	10012209
Irregular sleep phase	10022995
Irregular sleep wake rhythm disorder	10080301
Non-24-hour sleep-wake disorder	10078086
Shift work disorder	10078088

HLGT Sleep disturbances (incl subtypes)

PT	PT Code
Abnormal dreams	10000125
Abnormal sleep-related event	10061613
Confusional arousal	10067494
Loss of dreaming	10065085
Sleep inertia	10067493
Sleep paralysis	10041002
Sleep sex	10067492
Sleep talking	10041009
Sleep terror	10041010
Sleep-related eating disorder	10067315
Somnambulism	10041347
Behavioural insomnia of childhood	10072072
Hyposomnia	10067530
Initial insomnia	10022035
Insomnia	10022437
Middle insomnia	10027590
Terminal insomnia	10068932
Advanced sleep phase	10001423
Circadian rhythm sleep disorder	10009191
Delayed sleep phase	10012209
Irregular sleep phase	10022995
Irregular sleep wake rhythm disorder	10080301
Non-24-hour sleep-wake disorder	10078086
Shift work disorder	10078088
Cataplexy	10007737
Hypersomnia	10020765
Narcolepsy	10028713
Central-alveolar hypoventilation	10007982
Sleep apnoea syndrome	10040979

PT	PT Code
Breathing-related sleep disorder	10006344
Dyssomnia	10061827
Fatal familial insomnia	10072077
Microsleep	10076954
Periodic limb movement disorder	10064600
Pickwickian syndrome	10035004
Poor quality sleep	10062519
Rapid eye movement sleep behaviour disorder	10077299
Rapid eye movements sleep abnormal	10037841
Sleep deficit	10080881
Sudden onset of sleep	10050014
Upper airway resistance syndrome	10063968

12. Injection Site Reactions (ISR) from Study Drug Injections

Study drug ISR data available in the database, i.e. data collected from non-serious ISR AE eCRF form and collected serious adverse events with 'STUDY DRUG INJECTION SITE' included in the AE term.

13. Seizures and Seizure-like Events

Convulsions (SMQ)

PT	PT Code
2-Hydroxyglutaric aciduria	10078971
Acquired epileptic aphasia	10052075
Acute encephalitis with refractory, repetitive partial seizures	10076948
Alcoholic seizure	10056347
Aspartate-glutamate-transporter deficiency	10079140
Atonic seizures	10003628
Atypical benign partial epilepsy	10056699
Automatism epileptic	10003831
Autonomic seizure	10049612
Baltic myoclonic epilepsy	10054895
Benign familial neonatal convulsions	10067866
Benign rolandic epilepsy	10070530
Biotinidase deficiency	10071434
Change in seizure presentation	10075606
Clonic convulsion	10053398
Convulsion in childhood	10052391

PT	PT Code
Convulsion neonatal	10010911
Convulsions local	10010920
Convulsive threshold lowered	10010927
CSWS syndrome	10078827
Deja vu	10012177
Double cortex syndrome	10073490
Dreamy state	10013634
Drug withdrawal convulsions	10013752
Early infantile epileptic encephalopathy with burst-suppression	10071545
Eclampsia	10014129
Epilepsy	10015037
Epilepsy surgery	10079824
Epilepsy with myoclonic-atonic seizures	10081179
Epileptic aura	10015049
Epileptic psychosis	10059232
Febrile convulsion	10016284
Febrile infection-related epilepsy syndrome	10079438
Focal dyscognitive seizures	10079424
Frontal lobe epilepsy	10049424
Generalised non-convulsive epilepsy	10018090
Generalised tonic-clonic seizure	10018100
Glucose transporter type 1 deficiency syndrome	10078727
Gray matter heterotopia	10080533
Hemimegalencephaly	10078100
Hyperglycaemic seizure	10071394
Hypocalcaemic seizure	10072456
Hypoglycaemic seizure	10048803
Hyponatraemic seizure	10073183
Idiopathic generalised epilepsy	10071081
Infantile spasms	10021750
Juvenile myoclonic epilepsy	10071082
Lafora's myoclonic epilepsy	10054030
Lennox-Gastaut syndrome	10048816
Migraine-triggered seizure	10076676
Molybdenum cofactor deficiency	10069687
Multiple subpial transection	10079825
Myoclonic epilepsy	10054859
Myoclonic epilepsy and ragged-red fibres	10069825
Partial seizures	10061334

PT	PT Code
Partial seizures with secondary generalisation	10056209
Petit mal epilepsy	10034759
Polymicrogyria	10073489
Post stroke epilepsy	10076982
Post stroke seizure	10076981
Postictal headache	10052470
Postictal paralysis	10052469
Postictal psychosis	10070669
Postictal state	10048727
Post-traumatic epilepsy	10036312
Schizencephaly	10073487
Seizure	10039906
Seizure anoxic	10039907
Seizure cluster	10071350
Seizure like phenomena	10071048
Severe myoclonic epilepsy of infancy	10073677
Simple partial seizures	10040703
Status epilepticus	10041962
Sudden unexplained death in epilepsy	10063894
Temporal lobe epilepsy	10043209
Tonic clonic movements	10051171
Tonic convulsion	10043994
Tonic posturing	10075125
Topectomy	10073488
Transient epileptic amnesia	10081728
Tuberous sclerosis complex	10080584
Uncinate fits	10045476

PTs (Selective)

PT	PT Code
Confusional state	10010305
Loss of consciousness	10024855
Syncope	10042772
Sopor	10058709
Stupor	10042264
Altered state of consciousness	10050093
Depressed level of consciousness	10012373
Consciousness fluctuating	10050093

14. Weight Gain

HLT General nutritional disorders NEC (Selective)

PT	PT Code
Abdominal fat apron	10077983
Overweight	10033307
Abnormal weight gain	10000188
Central obesity	10065941
Obesity	10029883

HLT Physical examination procedures and organ system status (Selective)

PT	PT Code
Weight abnormal	10056814
Weight increased	10047899
Waist circumference increased	10064863
Body mass index abnormal	10074506
Body mass index increased	10005897

General signs and symptoms NEC (Selective)

PT	PT Code
Fat tissue increased	10016251

15. Rhabdomyolysis

Rhabdomyolysis/myopathy (SMQ)

PT	PT Code
Muscle necrosis	10028320
Myoglobin blood increased	10028625
Myoglobin blood present	10059888
Myoglobin urine present	10028631
Myoglobinaemia	10058735
Myoglobinuria	10028629
Myopathy	10028641
Myopathy toxic	10028648
Necrotising myositis	10074769

PT	PT Code
Rhabdomyolysis	10039020
Thyrotoxic myopathy	10081524

PTs (Selective)

PT	PT Code
Myalgia	10028411
Myositis	10028653

16. Pancreatitis

Acute pancreatitis (SMQ)

PT	PT Code
Cullen's sign	10059029
Grey Turner's sign	10075426
Haemorrhagic necrotic pancreatitis	10076058
Hereditary pancreatitis	10056976
Ischaemic pancreatitis	10066127
Oedematous pancreatitis	10052400
Pancreatic abscess	10048984
Pancreatic haemorrhage	10033625
Pancreatic necrosis	10058096
Pancreatic phlegmon	10056975
Pancreatic pseudoaneurysm	10081762
Pancreatic pseudocyst	10033635
Pancreatic pseudocyst drainage	10033636
Pancreatitis	10033645
Pancreatitis acute	10033647
Pancreatitis haemorrhagic	10033650
Pancreatitis necrotising	10033654
Pancreatitis relapsing	10033657
Pancreatorenal syndrome	10056277

17. Impact on Creatinine

Acute renal failure (SMQ)

PT	PT Code
Acute kidney injury	10069339
Acute phosphate nephropathy	10069688

PT	PT Code
Anuria	10002847
Azotaemia	10003885
Continuous haemodiafiltration	10066338
Dialysis	10061105
Foetal renal impairment	10078987
Haemodialysis	10018875
Haemofiltration	10053090
Hyponatriuria	10077515
Neonatal anuria	10049778
Nephropathy toxic	10029155
Oliguria	10030302
Peritoneal dialysis	10034660
Prerenal failure	10072370
Renal failure	10038435
Renal failure neonatal	10038447
Renal impairment	10062237
Renal impairment neonatal	10049776

Renal Failure and Impairment HLT

PT	PT Code
Acute Kidney injury	10069339
Anuria	10002847
Atypical haemolytic uraemic syndrome	10079840
Cardiorenal syndrome	10068230
Chronic kidney disease	10064848
Crush syndrome	10050702
Diabetic end stage renal disease	10012660
End stage renal disease	10077512
Foetal renal impairment	10078987
Haemolytic uraemic syndrome	10018932
Hepatorenal failure	10019845
Hepatorenal syndrome	10019846
Nail-patella syndrome	10063431
Neonatal anuria	10049778
Oliguria	10030302
Pancreatorenal syndrome	10056277
Postoperative renal failure	10056675
Postrenal failure	10059345
Prerenal failure	10072370

PT	PT Code
Propofol infusion syndrome	10063181
Renal failure	10038435
Renal failure neonatal	10038447
Renal impairment	10062237
Renal impairment neonatal	10049776
Renal injury	10061481
Scleroderma renal crisis	10062553
Traumatic anuria	10044501

18. Safety in Pregnancy

Use AE terms co-reported in pregnancy exposures to CAB and/or RPV.

15.12. Appendix 12: IDMC

Independent review will be provided by an IDMC 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. An ad-hoc review of data by the IDMC will be triggered whenever the number of confirmed virologic failures in the Q8W arm exceeds thresholds pre-specified in the IDMC charter. Further, analyses including futility checking will be performed for the IDMC to evaluate the efficacy and safety when approximately 50% of participants have completed their visit at Week 24.

The list of required outputs is provided in the IDMC Charter, Section 12.3, Appendix C.

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

15.12.1. Adhoc CVF IDMC Analyses

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

The Statistics Data Analysis Centre (SDAC) will be notified by the study virologist in writing every time a CVF occurs in the study. The SDAC will track the number of participants on Q8W arm 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).

15.12.2. Week 24 IDMC Analyses

Analyses including futility checking will be performed when approximately 50% of participants have completed their Week 24 visit.

A futility rule will assess the evidence that the CAB LA + RPV LA Q8W arm is non-inferior to the Q4W control arm. This rule will use the interim data (~ 50% participants completing Week 24) to calculate the Bayesian predictive probabilities that the CAB LA + RPV LA Q8W arm is non-inferior to the Q4W arm at Week 24. A 4% non-inferiority margin will be used. The details of statistical methods can be found in IDMC Charter, Section 12.6.1. The list of outputs is also provided in Section 15.14.4.

15.13. Appendix 13: Abbreviations & Trademarks

15.13.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AESI	Adverse Events of Special Interest
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
eC-SSRS	Electronic Columbia Suicide Severity Rating Scale
CVb	Coefficient of Variation (Between)
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
FDA	Food and Drug Administration
FSFV	First Subject First Visit
GSK	GlaxoSmithKline
GUI	Guidance
HAT-QoL	Health-related Quality of Life
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HIVTSQc	Change Version of HIV Treatment Satisfaction Questionnaire
HIVTSQs	Status Version of HIV Treatment Satisfaction Questionnaire
HLGT	High Level Group Term
HLT	High Level Term
HSR	Hypersensitivity Reaction
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
NA	Not Applicable
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
PIN	Perception of Injection
PK	Pharmacokinetic
PP	Per Protocol
PT	Preferred Term
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAMOS	Randomization & 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
SDRP	Study Results Dissemination Plan
SDTM	Study Data Tabulation Model
SMQ	Standardised MedDRA Query
SOC	System Organ Class
SOP	Standard Operation Procedure
TFL	Tables, Figures & Listings
TRDF	Treatment Related Discontinuation Failure

15.13.2. Trademarks

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15.14. Appendix 14: List of Data Displays

15.14.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

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

15.14.2. Mock Example Shell Referencing

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

The example mock-up displays from other reporting efforts will be named in the format: Study Number/HARP Reporting Effort/Output Type (T/ F/L)/Display Number, where T stands for Table, F stands for Figure and L stands for Listing. For example, the Table 1.1 from primary_02 reporting effort for Study 201585 will be named by 201585/primary_02/T1.1.

Other example mock-up displays will be named using the following format.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Pharmacokinetic / Pharmacodynamic	PKPD_Fn	PKPD_Tn	PK/PD_Ln
Health Outcomes	HO_Fn	HO_Tn	HO_Ln
Virology	VIR_Fn	VIR_Tn	VIR_Ln

NOTES:

- Non-Standard displays are indicated in the 'IDSL / Example Shell' or 'Programming Notes' column.

15.14.3. Deliverables

Delivery [1]	Description
IW24	IDMC analyses when approximately 50% participants have completed

Delivery [1]	Description
	their Week 24 visits
W24	Week 24 when 100% participants have completed their Week 24 visits
HL	Headline at Week 48
W48	Week 48
W96	Week 96
EOS	End of study

NOTES:
1. Indicates order in which displays will be generated for the reporting effort

15.14.4. List of Data Displays for Week 24 IDMC and Week 24 Planned Analyses

For Week 24 planned analyses, the Week 24 Futility population will be replaced by the Intent-to-Treat Exposed population. In addition, unless otherwise specified, present the listings by prior exposure to CAB+RPV (i.e. rederived randomization strata, 0, 1-24, >24 weeks, refer to Section 15.6.2 for calculation details) except for study population listings.

15.14.4.1. Study Population Tables

Study Population Tables						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition						
1.1	NA	Week 24 Futility	ES1	Summary of Subject Accountability: Maintenance Phase Conclusion Record - Week 24 Futility	ICH E3, GSKCTR, FDAAA, EudraCT, see also in 201585/primary_02/T1.7.	IW24
1.2	1.1	Intent-to-Treat Exposed	ES1	Summary of Subject Accountability: Maintenance Phase Conclusion Record - ITT-E	ICH E3, GSKCTR, FDAAA, EudraCT, see also in 201585/primary_02/T1.7.	IW24, W24
Demographic and Baseline Characteristics						
1.3	NA	Week 24 Futility	201585/primary_02/T1.16	Summary of Demographic Characteristics - Week 24 Futility	ICH E3, FDAAA, EudraCT	IW24
1.4	1.2	Intent-to-Treat Exposed	201585/primary_02/T1.16	Summary of Demographic Characteristics - ITT-E	ICH E3, FDAAA, EudraCT	IW24, W24
1.5	NA	Week 24 Futility	201584/idmc_03/T1.3	Summary of Prior Exposure to CAB+RPV - Week 24 Futility	Adjust footnote and row labels as appropriate.	IW24
1.6	1.3	Intent-to-Treat Exposed	201584/idmc_03/T1.3	Summary of Prior Exposure to CAB+RPV - ITT-E	Adjust footnote and row labels as appropriate.	IW24, W24
1.7	1.4	Intent-to-Treat Exposed	201584/idmc_03/T1.7	Summary of Prior Exposure to CAB+RPV by Country	Adjust footnote and row labels as appropriate.	IW24, W24
1.8	1.5	Intent-to-Treat Exposed	201585/primary_02/T1.19	Summary of Hepatitis Status at Entry	Add footnote as appropriate for subjects classified as Hepatitis B positive in analysis.	IW24, W24

15.14.4.2. Efficacy Tables

Efficacy Tables						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.1	2.1	Week 24 Futility	201585/primary_02/T2.1	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA ≥50 c/mL at Week 24 and Posterior Predictive Probability of Success for the Q8W Arm - Snapshot Analysis	For Week 24 IDMC, add a column on right with 'Posterior Predictive Probability of Success" and adjust the footnotes as appropriate, also add a footnote “Target threshold for posterior predictive probability is 15%.”. For planned Week 24, remove ‘and Posterior Predictive Probability of Success for the Q8W Arm’ from the title, adjust the footnote as appropriate. For proportions, keep one decimal place. The adjustment is based on rederived randomization strata.	IW24, W24
2.2	2.2	Week 24 Futility	201585/primary_02/T2.4	Summary of Study Outcomes (50 c/mL Threshold) at Week 24 (Maintenance Phase) - Snapshot Analysis	For proportions, keep one decimal place.	IW24, W24
2.3	2.3	Week 24 Futility	201585/primary_02/T2.6	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA ≥50 c/mL at Week 24 by Randomization Strata (Maintenance Phase) - Snapshot Analysis	Note that only by randomization strata summary is provided. Change the footnote to “[1] Difference: Proportion on Q8W - Proportion on Q4W. 95% CIs were calculated using an unconditional exact method with two inverted one-sided tests based on the score statistic.” Add Footnote "Note: Randomization strata are rederived using the prior exposure to CAB+RPV in Study 201585, collected from eCRF." For proportions, keep one decimal place.	IW24, W24

Efficacy Tables						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.4	2.4	Week 24 Futility	201585/primary_02/T2.21	Cumulative Proportion of Subjects Meeting Confirmed Virologic Failure by Visit (Up to Week 24)	For proportions, keep one decimal place. Non-snapshot visit window will be used.	IW24, W24
2.5	2.5	Week 24 Futility	201585/primary_02/T2.21	Cumulative Proportion of Subjects Meeting Confirmed Virologic Failure by Visit and Randomization Strata (Up to Week 24)	Add column for 'Analysis Strata', add footnote for randomization strata similar to T2.3. For proportions, keep one decimal place. Non-snapshot visit window will be used.	IW24, W24
2.6	2.6	Intent-to-Treat Exposed	201585/primary_02/T2.21	Cumulative Proportion of Subjects Meeting Confirmed Virologic Failure during the Maintenance Phase	Note that this is overall summary, not by visit. Replace the column 'Timepoint' with 'CVF Category'. For proportions, keep one decimal place.	IW24, W24
2.7	2.7	Intent-to-Treat Exposed	201584/idmc_03/T2.7	Cumulative Proportion of Subjects Meeting Confirmed Virologic Failure by Randomization Strata during the Maintenance Phase	Adjust footnote and row labels as appropriate. For proportions, keep one decimal place. Use rederived Randomization strata.	IW24, W24
2.8	2.8	Week 24 Futility	EFF_T1	Summary of Kaplan-Meier Estimates of Proportion of Subjects without CVF at Week 24 - Treatment Related Discontinuation = Failure	The non-snapshot visit window for Week 24 will be used.	IW24, W24

Efficacy Tables						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.9	2.9	Week 24 Futility	EFF_T2	Summary of Kaplan-Meier Estimates of Proportion of Subjects without CVF at Week 24 - Efficacy Related Discontinuation=Failure	The non-snapshot visit window for Week 24 will be used.	IW24, W24
2.10	2.10	Intent-to-Treat Exposed	201584/idmc_03/T2.10	Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL by Visit - Observed Case Analysis	Adjust the footnote as appropriate. The non-snapshot visit window will be used. For W24, add '(Up to Week 24)' to the title, only display visits up to Week 24.	IW24, W24
2.11	2.11	Intent-to-Treat Exposed	201584/idmc_03/T2.11	Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Visit and Randomization Strata - Observed Case Analysis	Adjust footnote and row labels as appropriate. The non-snapshot visit window and rederived randomization strata will be used. For W24, add '(Up to Week 24)' to the title, only display visits up to Week 24.	IW24, W24

15.14.4.3. Efficacy Figures

Efficacy Figures						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.1	2.1	Week 24 Futility	201584/idmc_03/F2.1	Individual Plasma HIV-1 RNA (log10 c/mL) Profiles by Visit for Subjects Who are in the Category of 'Viral Load ≥50 c/mL' at Week 24 per Snapshot Algorithm	Adjust the x-axis label and footnote as appropriate. The x-values are based on study day of the assessment.	IW24, W24
2.2	2.2	Intent-to-Treat Exposed	201584/idmc_03/F2.2	Individual Plasma HIV-1 RNA (log10 c/mL) Profiles by Visit for Subjects with a Viral Load ≥50 c/mL during the Maintenance Phase	Adjust the x-axis label and footnote as appropriate. The x-values are based on study day of the assessment.	IW24, W24

15.14.4.4. Safety Tables

Safety Tables						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Adverse Events						
3.1	3.1	Safety	AE3	Summary of All Adverse Events by Overall Frequency - Maintenance Phase	See also in 201585/primary_02/T3.20.	IW24, W24
3.2	3.2	Safety	AE1	Summary of All Drug-Related Adverse Events by System Organ Class - Maintenance Phase	See also in 201585/primary_02/T3.16.	IW24, W24
3.3	3.3	Safety	AE3	Summary of Grade 3-5 Adverse Events by Overall Frequency - Maintenance Phase	See also in 201585/primary_02/T3.20.	IW24, W24
Serious and Other Significant Adverse Events						
3.4	3.4	Safety	AE1	Summary of Serious Adverse Events by System Organ Class - Maintenance Phase	See also in 201585/primary_02/T3.21.	IW24, W24
3.5	3.5	Safety	AE1	Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by System Organ Class - Maintenance Phase	See also in 201585/primary_02/T3.31.	IW24, W24
Injection Site Reaction Adverse Events						
3.6	3.6	Safety	201585/primary_02/T3.40	Summary of Injection Site Reaction Adverse Events (Event-Level Summary) - Maintenance Phase	For W24, add ‘Study Drug’ before ‘Injection’ in the title and only summarize ISR from study drug injections.	IW24, W24

Safety Tables						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.7	3.7	Safety	201585/primary_02/T3.43	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events - Overall and Common (Maintenance Phase)	Common ISR adverse events includes injection site pain, injection site induration, injection site nodules and any other ISR with ≥5% subjects in either treatment arm. For W24, add 'Study Drug' before 'Injection' in the title and only summarize ISR from study drug injections.	IW24, W24
Laboratory: Chemistry and Hematology						
3.8	3.8	Safety	201584/idmc_03/T3.8	Summary of Maximum Post-Baseline Emergent Clinical Chemistry Toxicities Parameters of Special Interest - Maintenance Phase	Replace "Day 1" with "Study Day 1" in the first footnote. Use the same parameter list as the one in 201584/idmc_03/T3.8.	IW24, W24
3.9	3.9	Safety	201584/idmc_03/T3.9	Summary of Maximum Post-Baseline Emergent Hematology Toxicities Parameters of Special Interest - Maintenance Phase	Replace "Day 1" with "Study Day 1" in the first footnote. Adjust the second footnote to be: "Note: Parameters of Special Interest include Hemogoblin, Leukocytes, Neutrophils, and Platelets." In output, change the parameter label 'White Blood Cell count' to 'Leukocytes'.	IW24, W24

15.14.4.5. Safety Figures

Safety Figures						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Laboratory: Hepatobiliary (Liver)						
3.1	3.1	Safety	201584/idmc_03/F3.2	Scatter Plot of Maximum Maintenance Phase vs. Baseline for ALT	Adjust the legend as needed. Change the first footnote to “Axes are on a log10 scale”. Remove the second footnote. Adjust the treatment label from empty triangle to solid triangle.	IW24, W24
3.2	3.2	Safety	201584/idmc_03/F3.1	Matrix Plot of Maximum Liver Chemistries - Maintenance Phase	Replace “>5.1” with “>5.0” in the second footnote. Make treatment labels in the plot consistent across figures.	IW24, W24

15.14.4.6. Pharmacokinetic Tables

Pharmacokinetic Tables						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
4.1	4.1	Pharmacokinetic	201585/primary_02/T4.1	Summary of Plasma CAB PK Concentrations (ug/mL) - Time Data by Treatment and Visit - Including Log-Transformed Statistics	Remove the first footnote “Note:…”.	IW24, W24
4.2	4.2	Pharmacokinetic	201585/primary_02/T4.2	Summary of Plasma RPV PK Concentrations (ng/mL) - Time Data by Treatment and Visit - Including Log-Transformed Statistics	Remove the first footnote “Note:…”..	IW24, W24
4.3	NA	Pharmacokinetic	201584/idmc_03/T4.3	Proportion of Subjects with Evaluable PK Concentration below Expected Values		IW24

15.14.4.7. Pharmacokinetic Figures

Pharmacokinetic Figures						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
4.1	NA	Pharmacokinetic	201584/idmc_03/ F4.1	Scatter Plot of Evaluable PK Concentrations in Relation to Occurrence of CVF up to Week 16 for Subjects on Q8W Arm by Visit and Randomization Strata	Note that this plot is by visit and rederived randomization strata. Add footnote for strata as appropriate.	IW24

15.14.4.8. Virology Tables

Virology Tables						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
7.1	7.1	Confirmed Virologic Failure	201585/primary_02/T8.1	Summary of the Prevalence of Known INI Resistance Mutations at Time of CVF (Maintenance Phase) - Plasma Sample		IW24, W24
7.2	7.2	Confirmed Virologic Failure	201585/primary_02/T8.2	Summary of the Prevalence of Major Resistance Mutations of NNRTI, NRTI, and PI Class at Time of CVF (Maintenance Phase) - Plasma Sample		IW24, W24
7.3	7.3	Confirmed Virologic Failure	201585/primary_02/T8.3	Summary of Phenotypic Susceptibility at Time of CVF (Maintenance Phase) - Plasma Sample		IW24, W24
7.4	7.4	Confirmed Virologic Failure	201585/primary_02/T8.7	Summary of Fold Change to CAB and RPV at Time of CVF (Maintenance Phase) - Plasma Sample		IW24, W24
7.5	7.5	Confirmed Virologic Failure	201585/primary_02/T8.8	Summary of Viral Load, Genotypic and Phenotypic Data for Subjects Who Met Confirmed Virologic Failure Criteria during the Maintenance Phase	Remove the Columns ‘ARTs’ and ‘FC for ARTs’. Remove the footnotes [1] and [2]. Adjust the footnote as appropriate.	IW24, W24

15.14.4.9. ICH Listings

Note: Both unique subject ID and latest subject ID for a subject will be included in the listings, unless otherwise specified.

ICH Listings						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Study Population						
1	1	Randomized	201584/idmc_03/L1.3	Listing of Randomized and Actual Strata and Treatment Assignment	Randomized and Actual Treatments will include oral lead-in information (e.g. Oral followed by Q4W). For W24 analyses, remove column for Futility Population.	IW24, W24
Efficacy						
2	2	Week 24 Futility	201585/primary_02/L11	Listing of Study Outcomes (50 c/mL Threshold) at Week 24 - Snapshot Analysis		IW24, W24
Adverse Events						
3	3	Safety	201585/primary_02/L17	Listing of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product - Maintenance Phase	Remove “Time Since Last Dose” from the column header.	IW24, W24
4	4	Safety	201585/primary_02/L17	Listing of All Serious Adverse Events - Maintenance Phase	Remove “Time Since Last Dose” from the column header.	IW24, W24
Laboratory						
5	NA	Safety	201584/idmc_03/L3.5	Listing of All Parameters of Special Interest Laboratory Data for Subjects with Grade 3 or 4 Maintenance Phase Emergent Toxicities for Parameters of Special Interest	Replace ‘Day 1’ with ‘Study Day 1’ in the second footnote.	IW24

ICH Listings						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
PK						
6	5	Pharmacokinetic	201584/idmc_03/L4.1	Listing of Plasma CAB PK Concentration-Time Data	Change the first footnote to "Relative Time is calculated relative to the date and time of last previous dose. If the time of the last previous dose (e.g. oral lead-in/oral-bridging) is missing, then the relative time will be set to missing and the sample will not be considered 'evaluable'." Remove the second footnote. Change column header 'Visit' to 'Analysis Visit/Nominal Visit' to include both visits.	IW24, W24
7	6	Pharmacokinetic	201584/idmc_03/L4.2	Listing of Plasma RPV PK Concentration-Time Data	Change the first footnote to "Relative Time is calculated relative to the date and time of last previous dose. If the time of the last previous dose (e.g. oral lead-in/oral-bridging) is missing, then the relative time will be set to missing and the sample will not be considered 'evaluable'." Remove the second footnote. Change column header 'Visit' to 'Analysis Visit/Nominal Visit' to include both visits.	IW24, W24

15.14.4.10. Non-ICH Listings

Note: Both unique subject ID and latest subject ID for a subject will be included in the listings, unless otherwise specified.

Non-ICH Listings						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Study Population						
8	7	Intent-to-Treat Exposed	ES2	Listing of Reasons for Maintenance Phase Withdrawal	See also in 201585/primary_02/L30.	IW24, W24
9	8	Screened	Shell POP_L2	Listing of Subjects Who Were Rescreened		IW24, W24
10	9	Intent-to-Treat Exposed	201584/idmc_03/L1.1	Listing of Prior Antiretroviral Therapy	Remove the column 'Treatment Phase/Treatment State'. Add a column for Route.	IW24, W24
11	10	Intent-to-Treat Exposed	201584/idmc_03/L1.2	Listing of Concomitant Antiretroviral Therapy	Change column 'Treatment Phase/Actual Treatment State' to 'Phase during Which Concomitant', remove 'Induction Study Day' from column headers, and remove 'Maintenance' from 'Maintenance Study Day' in column headers.	IW24, W24
Efficacy						
12	11	Confirmed Virologic Failure	201585/primary_02/L40	Listing of All Plasma HIV-1 RNA Viral Load Data for Subjects with Confirmed Virologic Failure during the Maintenance Phase	Non-snapshot visit window will be used for deriving the visits in Column 'Actual Relative Time'. Replace 'Period' in column header with 'Phase'.	IW24, W24

Non-ICH Listings						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
13	12	Week 24 Futility	201585/primary_02/L40	Listing of All Plasma HIV-1 RNA Viral Load Data for Subjects Who are in the Category of 'Viral load ≥50 c/mL' at Week 24 per Snapshot Algorithm	Non-snapshot visit window will be used for deriving the visits in Column 'Actual Relative Time'. Replace 'Period' in column header with 'Phase'.	IW24, W24
Adverse Events						
14	13	Safety	201585/primary_02/L17	Listing of All Drug-Related Adverse Events - Maintenance Phase	Remove "Time Since Last Dose" from the column header.	IW24, W24
15	14	Safety	201585/primary_02/L17	Listing of All Grade 3-5 Adverse Events - Maintenance Phase	Remove "Time Since Last Dose" from the column header.	IW24, W24
16	15	Safety	201585/primary_02/L17	Listing of All Adverse Events - Long-term Follow-up Phase	Remove "Time Since Last Dose" from the column header.	IW24, W24
PK						
17	NA	Pharmacokinetic	201584/idmc_03/L4.3	Listing of Plasma CAB PK Concentration-Time Data for Subjects with CAB Concentration <1.35 ug/mL (~8 X PAIC90) at Visits up to Week 16	Change the first footnote to "Relative Time is calculated relative to the date and time of last previous dose. If the time of the last previous dose (e.g. oral lead-in/oral-bridging) is missing, then the relative time will be set to missing and the sample will not be considered 'evaluable'." Remove the second footnote. Change column header 'Visit' to 'Analysis Visit/Nominal Visit' to include both visits.	IW24

Non-ICH Listings						
No. in IW24	**No. in W24**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
18	NA	Pharmacokinetic	201584/idmc_03/L4.4	Listing of Plasma CAB PK Concentration-Time Data for Subjects with CAB Concentration <0.166 ug/mL (PAIC90) at Visits up to Week 16	The same note as in Listing 17.	IW24
19	NA	Pharmacokinetic	201584/idmc_03/L4.5	Listing of Plasma RPV PK Concentration-Time Data for Subjects with RPV Concentration <12 ng/mL (PAIC90) at Visits up to Week 16	The same note as in Listing 17.	IW24
Virology						
20	16	Confirmed Virologic Failure	201584/idmc_03/L7.1	Listing of Genotypic Mutation Data at All Timepoints		IW24, W24
21	17	Confirmed Virologic Failure	201584/idmc_03/L7.2	Listing of Phenotypic Data at All Timepoints		IW24, W24

15.14.5. List of Data Displays for Week 48/96/End-of-Study Planned Analyses

15.14.5.1. Study Population Tables

Study Population Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition							
1.1	1.1	1.1	Randomized	NS1	Summary of Number of Subjects Enrolled by Country and Site ID	'No Treatment' column is not needed.	W48, W96, EOS
1.2	1.2	1.2	Screened	ES6	Summary of Screening Status and Reasons for Screening Failures		W48, W96, EOS
1.3	1.3	1.3	Intent-to-Treat Exposed	ES1	Summary of Subject Accountability: Study Conclusion Record		W48, W96, EOS
1.4	1.4	NA	Intent-to-Treat Exposed	ES1	Summary of Subject Accountability: Maintenance Phase Conclusion Record		HL, W48, W96
NA	1.5	1.4	Intent-to-Treat Exposed	ES1	Summary of Subject Accountability: Maintenance + Extension Phase Conclusion Record	For subject status, include 'ONGOING', 'COMPLETED MAINTENANCE PHASE', 'COMPLETED EXTENSION PHASE', 'WITHDRAWN FROM MAINTENANCE PHASE' and 'WITHDRAWN FROM EXTENSION PHASE'.	W96, EOS
1.5	1.6	1.5	Long-term Follow-up	ES1	Summary of Subject Accountability: Long-term Follow-up Phase Conclusion Record		W48, W96, EOS

Study Population Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.6	1.7	1.6	Intent-to-Treat Exposed	ES4	Summary of Subject Disposition at Each Study Phase	Replace 'Epoch' with 'Phase' in column header. Screening Phase will not be included. Add a footnote "Note: Entry into Long-Term Follow-up is based on presence of a long-term follow-up visit in the eCRF (i.e. LTFU Month 1, LTFU Month 3, etc.) or evidence of filling out the long-term follow-up phase conclusion form."	W48, W96, EOS
1.7	1.8	1.7	Intent-to-Treat Exposed	ES5	Summary of Reasons for Withdrawal at Each Study Phase	The same comment as above.	W48, W96, EOS
1.8	1.9	1.8	Intent-to-Treat Exposed	201584/primary_01/T1.9	Summary of Subject Accountability: Withdrawals by Visit (Maintenance + Extension Phase)	.	W48, W96, EOS
1.9	1.10	1.9	Intent-to-Treat Exposed	ES1	Summary of Study Drug Discontinuation	Update the row label to 'Primary Reason[1]/Subreason[2] for Study Drug Discontinuation'.	W48, W96, EOS
1.10	1.11	NA	Intent-to-Treat Exposed	DV1a	Summary of Important Protocol Deviations (Maintenance Phase)		W48, W96
NA	1.12	1.10	Intent-to-Treat Exposed	DV1a	Summary of Important Protocol Deviations (Maintenance + Extension Phase)		W96, EOS
1.11	1.13	1.11	Intent-to-Treat	IE1	Summary of Inclusion/Exclusion Criteria		W48, W96, EOS

Study Population Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
			Exposed		Deviations		
1.12	1.14	1.12	Screened	201585/primary_02/T1.1	Summary of Study Populations	Adjust the footnote as appropriate.	HL, W48, W96, EOS
1.13	1.15	NA	Intent-to-Treat Exposed	201585/primary_02/T1.14	Summary of Protocol Deviations Leading to Exclusion from the Per-Protocol Population (through Maintenance Phase)		W48, W96
Demographic and Baseline Characteristics							
1.14	1.16	1.13	Intent-to-Treat Exposed	201585/primary_02/T1.16	Summary of Demographic Characteristics		HL, W48, W96, EOS
1.15	1.17	1.14	Randomized	DM11	Summary of Age Ranges	Also refer to 201585/primary_02/T1.4. Follow the footnote in 201585/primary_02/T1.4.	W48, W96, EOS
1.16	1.18	1.15	Intent-to-Treat Exposed	DM5	Summary of Race and Racial Combinations		W48, W96, EOS
1.17	1.19	1.16	Intent-to-Treat Exposed	DM6	Summary of Race and Racial Combinations Details		W48, W96, EOS
1.18	1.20	1.17	Intent-to-Treat Exposed	201585/primary_02/T1.19	Summary of Hepatitis Status at Entry	Add footnote as appropriate for subjects classified as Hepatitis B positive in analysis.	W48, W96, EOS
1.19	1.21	1.18	Intent-to-Treat Exposed	201585/primary_02/T1.20	Summary of Derived Baseline CDC Stages of HIV Infection		W48, W96, EOS

Study Population Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.20	1.22	1.19	Intent-to-Treat Exposed	201585/primary_02/T1.21	Summary of Baseline Cardiovascular Risk Assessments		W48, W96, EOS
1.21	1.23	1.20	Intent-to-Treat Exposed	201585/primary_02/T1.22	Distribution of CD4+ Cell Count Results at Screening and Baseline		W48, W96, EOS
1.22	1.24	1.21	Intent-to-Treat Exposed	Shell POP_T1	Summary of Prior Exposure to CAB+RPV		W48, W96, EOS
1.23	1.25	1.22	Intent-to-Treat Exposed	201585/primary_02/T1.36	Summary of HIV Risk Factors		W48, W96, EOS
Medical Conditions and Medications							
1.24	1.26	1.23	Intent-to-Treat Exposed	MH1	Summary of Current Medical Conditions		W48, W96, EOS
1.25	1.27	1.24	Intent-to-Treat Exposed	MH1	Summary of Past Medical Conditions		W48, W96, EOS
1.26	1.28	1.25	Intent-to-Treat Exposed	MH4	Summary of Current Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, Nervous System Conditions, and Hepatobiliary Disorders		W48, W96, EOS
1.27	1.29	1.26	Intent-to-Treat Exposed	MH4	Summary of Past Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, Nervous System Conditions, and Hepatobiliary Disorders		W48, W96, EOS

Study Population Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.28	1.30	1.27	Intent-to-Treat Exposed	201585/primary_02/T1.28	Summary of Prior ART Medications	Remove the footnote. Follow definitions in Section 6.2 to determine the prior ART medications.	W48, W96, EOS
1.29	1.31	NA	Intent-to-Treat Exposed	CM8	Summary of Concomitant Non-ART Medication Ingredient Combinations (Maintenance Phase)		W48, W96
NA	1.32	1.28	Intent-to-Treat Exposed	CM8	Summary of Concomitant Non-ART Medication Ingredient Combinations (Maintenance + Extension Phase)		W96, EOS
1.30	1.33	1.29	Intent-to-Treat Exposed	201585/primary_02/T1.33	Summary of Lipid Modifying Agent Use at Baseline		W48, W96, EOS
1.31	1.34	1.30	Intent-to-Treat Exposed	201585/primary_02/T1.34	Summary of Lipid Modifying Agent Use Started during the Maintenance Phase		W48, W96, EOS
1.32	1.35	1.31	Intent-to-Treat Exposed	201585/primary_02/T1.35	Summary of Substance Use at Entry		W48, W96, EOS

15.14.5.2. Efficacy Tables

Note: For subgroup analyses, include rederived randomization strata (i.e. prior exposure to CAB+RPV: 0, 1-24, >24 weeks), all demographic and baseline characteristic subgroups as mentioned in EMA Subgroup Category 2 in Section 5.4.2, unless otherwise specified. Not all subjects on Q8W arm are planned to have viral load data collected at Week 4 (Week 4A or 4B), so leave Week 4 data blank for Q8W arm in by-visit snapshot analysis.

Efficacy Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Primary Efficacy Analyses							
2.1	2.1	NA	Intent-to-Treat Exposed	201584/primary_01/T2.1	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL at Week 48 (Maintenance Phase) – Snapshot Analysis – ITT-E	Adjust the footnotes as appropriate. For WK96, replace 'Week 48' with 'Week 96' in title.	HL, W48, W96
2.2	2.2	NA	Per-Protocol	201584/primary_01/T2.2	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL at Week 48 (Maintenance Phase) – Snapshot Analysis – Per-Protocol	Adjust the footnotes as appropriate. For WK96, replace 'Week 48' with 'Week 96' in title.	HL, W48, W96
2.3	2.3	NA	Intent-to-Treat Exposed	201584/primary_01/T2.3	Summary of Study Outcomes (50 c/mL Threshold) at Week 48 (Maintenance Phase) – Snapshot Analysis	For WK96, replace 'Week 48' with 'Week 96' in title.	HL, W48, W96
2.4	2.4	NA	Intent-to-Treat Exposed	Shell EFF_T3	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 WK96, replace 'Week 48' with 'Week 96' in title.	HL, W48, W96

Efficacy Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.5	2.5	NA	Intent-to-Treat Exposed	201584/primary_01/T2.5	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL at Week 48 by Subgroup (Maintenance Phase) - Snapshot Analysis	Adjust the footnote/column header label as appropriate. For WK96, replace 'Week 48' with 'Week 96' in title. Do not include rederived randomization strata in the table.	W48, W96
2.6	2.6	NA	Intent-to-Treat Exposed	Shell EFF_T4	Treatment by Strata Tests of Homogeneity for Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL at Week 48 among Subjects with >=1 Weeks Prior Exposure to CAB+RPV (Maintenance Phase) - Snapshot Analysis	For WK96, replace 'Week 48' with 'Week 96' in title.	W48, W96
2.7	2.7	NA	Intent-to-Treat Exposed	201584/primary_01/T2.6	Summary of Study Outcomes (50 c/mL Threshold) at Week 48 by Subgroup (Maintenance Phase) – Snapshot Analysis	For WK96, replace 'Week 48' with 'Week 96' in title.	W48, W96
Secondary and Exploratory Efficacy Analyses							
2.8	2.8	NA	Intent-to-Treat Exposed	201584/primary_01/T2.7	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 (Maintenance Phase) – Snapshot Analysis – ITT-E	Adjust the footnotes as appropriate. For WK96, replace 'Week 48' with 'Week 96' in title.	HL, W48, W96
2.9	2.9	NA	Per-Protocol	201584/primary_01/T2.8	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 (Maintenance Phase) – Snapshot Analysis – Per-Protocol	Adjust the footnotes as appropriate. For WK96, replace 'Week 48' with 'Week 96' in title.	HL, W48, W96

Efficacy Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.10	2.10	NA	Intent-to-Treat Exposed	Shell EFF_T3	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	Replace 'Number of HIV-1 RNA >=50 c/mL' with 'Number of HIV-1 RNA <50 c/mL' in column header. For WK96, replace 'Week 48' with 'Week 96' in title.	HL, W48, W96
2.11	2.11	NA	Intent-to-Treat Exposed	201584/primary_01/T2.10	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 by Subgroup (Maintenance Phase) - Snapshot Analysis	Adjust the footnote/column header label as appropriate. For WK96, replace 'Week 48' with 'Week 96' in title. Do not include rederived randomization strata in the table.	W48, W96
2.12	2.12	NA	Intent-to-Treat Exposed	Shell EFF_T4	Treatment by Strata Tests of Homogeneity for Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL at Week 48 among Subjects with >=1 Weeks Prior Exposure to CAB+RPV (Maintenance Phase) - Snapshot Analysis	Replace 'Number of HIV-1 RNA >=50 c/mL' with 'Number of HIV-1 RNA <50 c/mL' in column header. For WK96, replace 'Week 48' with 'Week 96' in title.	W48, W96
2.13	2.13	NA	Intent-to-Treat Exposed	201584/primary_01/T2.11	Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		W48, W96
2.14	2.14	NA	Intent-to-Treat Exposed	201584/primary_01/T2.12	Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL by Subgroup and Visit (Maintenance Phase) – Snapshot Analysis		W48, W96
2.15	2.15	NA	Intent-to-Treat Exposed	201584/primary_01/T2.15	Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		W48, W96

Efficacy Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.16	2.16	NA	Intent-to-Treat Exposed	201584/primary_01/T2.16	Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Subgroup and Visit (Maintenance Phase) – Snapshot Analysis		W48, W96
2.17	2.17	NA	Intent-to-Treat Exposed	201584/primary_01/T2.17	Proportion of Subjects with Plasma HIV-1 RNA <200 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		W48, W96
2.18	2.18	NA	Intent-to-Treat Exposed	201584/primary_01/T2.17	Proportion of Subjects with Plasma HIV-1 RNA >=200 c/mL by Visit (Maintenance Phase) – Snapshot Analysis	Adjust column headers as appropriate. Keep one decimal place for proportion.	W48, W96
2.19	2.19	NA	Intent-to-Treat Exposed	Shell EFF_T1	Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Failure at Week 48 - Treatment Related Discontinuation = Failure	Adjust the row labels and footnotes as appropriate. For WK96, replace 'Week 48' with 'Week96' in title.	W48, W96
2.20	2.20	NA	Intent-to-Treat Exposed	Shell EFF_T2	Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Failure at Week 48 - Efficacy Related Discontinuation = Failure	Adjust the row labels and footnotes as appropriate. For WK96, replace 'Week 48' with 'Week96' in title.	W48, W96
2.21	2.21	NA	Intent-to-Treat Exposed	201585/primary_02/T2.19	Proportion of Subjects with HIV-1 RNA >=50 c/mL at Week 48 (Snapshot) by Last Delay in IP Injection (Maintenance Phase)	Display both arms. Change the footnote to '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 did not receive Week 48 injection (i.e. missing visit or withdrawal)..'. For WK96, replace 'Week 48' with 'Week96' in title.	W48, W96

Efficacy Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.22	2.22	2.1	Intent-to-Treat Exposed	201585/primary_02/T2.20	Summary of Plasma HIV-1 RNA (log10 c/mL) by Visit		W48, W96, EOS
2.23	2.23	NA	Intent-to-Treat Exposed	201585/primary_02/T2.21	Cumulative Proportion of Subjects Meeting Confirmed Virology Failure Criteria by Visit during the Maintenance Phase (Up to Week 48)	For WK96, replace 'Up to Week 48' with 'Up to Week 96' in title.	HL, W48, W96
2.24	2.24	2.2	Intent-to-Treat Exposed	201584/primary_01/T2.21	Cumulative Proportion of Subjects Meeting Confirmed Virology Failure Criteria (Maintenance + Extension Phase)		W48, W96, EOS
2.25	2.25	NA	Intent-to-Treat Exposed	201584/primary_01/T2.24	Distribution of Quantitative Plasma HIV-1 RNA Results at Suspected and Confirmation of Confirmed Virologic Failure (Maintenance Phase)		W48, W96
2.26	2.26	NA	Intent-to-Treat Exposed	201585/primary_02/T2.34	Proportion of Subjects with Plasma HIV-1 RNA <2 c/mL by Visit (Maintenance Phase)	Change footnote to 'Note: Data come from BioMontr low-level assay. Only visits with available data from this assay are included.'	W48, W96
2.27	2.27	NA	Intent-to-Treat Exposed	201584/primary_01/T2.51	Summary of Study Outcomes (200 c/mL Threshold) at Week 48 (Maintenance Phase) – Snapshot Analysis	For WK96, replace 'Week 48' with 'Week 96' in title.	W48, W96
2.28	2.28	NA	Intent-to-Treat Exposed	201585/primary_02/T2.37	Summary of Subjects per Viral Load Category by Visit (Maintenance Phase)	Refer to 'Summary for Participants per Viral Load Category by Visit' in Section 15.6.3. Remove footnote [2]. Add a footnote "Note: The visit windows are based on snapshot analysis windows'.	W48, W96

Efficacy Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.29	2.29	2.3	Intent-to-Treat Exposed	201585/primary_02/T2.25	Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) by Visit (Maintenance + Extension Phase)		W48, W96, EOS
2.30	2.30	NA	Intent-to-Treat Exposed	201585/primary_02/T2.38	Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) at Week 48 by Subgroup (Maintenance Phase)	For WK96, replace 'Week 48' with 'Week 96' in title.	W48, W96
2.31	2.31	2.4	Intent-to-Treat Exposed	201585/primary_02/T2.26	Summary of CD4+ Cell Count (cells/mm^3) by Visit (Maintenance + Extension Phase)		W48, W96, EOS
2.32	2.32	2.5	Intent-to-Treat Exposed	201585/primary_02/T2.28	Summary of Change from Baseline in CD8+ Cell Count (cells/mm^3) by Visit (Maintenance + Extension Phase)		W48, W96, EOS
2.33	2.33	2.6	Intent-to-Treat Exposed	201585/primary_02/T2.27	Summary of CD8+ Cell Count (cells/mm^3) by Visit (Maintenance + Extension Phase)		W48, W96, EOS
2.34	2.34	2.7	Intent-to-Treat Exposed	201585/primary_02/T2.29	Summary of CD4+/CD8+ Ratio Cell Count (cells/mm^3) by Visit (Maintenance + Extension Phase)	Ratio will be taken when both CD4+ and CD8+ are available on the same date.	W48, W96, EOS
2.35	2.35	NA	Intent-to-Treat Exposed	201585/primary_02/T2.30	Summary of HIV-1 Associated Conditions Including Recurrences (Maintenance Phase)		W48, W96
NA	2.36	2.8	Intent-to-Treat Exposed	201585/primary_02/T2.30	Summary of HIV-1 Associated Conditions Including Recurrences (Maintenance +Extension Phase)		W96, EOS
2.36	2.37	NA	Intent-to-Treat Exposed	201585/primary_02/T2.31	Summary of HIV-1 Associated Conditions Excluding Recurrences (Maintenance Phase)		W48, W96

Efficacy Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
NA	2.38	2.9	Intent-to-Treat Exposed	201585/primary_02/T2.31	Summary of HIV-1 Associated Conditions Excluding Recurrences (Maintenance +Extension Phase)		W96, EOS
2.37	2.39	NA	Intent-to-Treat Exposed	201584/primary_01/T2.47	Summary of HIV-1 Disease Progression and/or Deaths (Maintenance Phase)		W48, W96
NA	2.40	2.10	Intent-to-Treat Exposed	201584/primary_01/T2.47	Summary of HIV-1 Disease Progression and/or Deaths (Maintenance + Extension Phase)		W96, EOS

15.14.5.3. Efficacy Figures

Note: For subgroup analyses, include rederived randomization strata (i.e. prior exposure to CAB+RPV: 0, 1-24, >24 weeks), all demographic and baseline characteristic subgroups as mentioned in EMA Subgroup Category 2 in Section 5.4.2, unless otherwise specified. Not all subjects on Q8W arm are planned to have viral load data collected at Week 4 (Week 4A or 4B), so leave Week 4 data blank for Q8W arm in by-visit snapshot analysis.

Efficacy Figures							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Primary Efficacy Analyses							
2.1	2.1	NA	Intent-to-Treat Exposed	201585/primary_02/F2.1	Proportion (95% CI) of Subjects with HIV-1 RNA ≥50 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		HL, W48, W96
2.2	2.2	NA	Intent-to-Treat Exposed	201584/primary_01/F2.2	Unadjusted Treatment Difference in Proportion (95% CI) of Subjects with HIV-1 RNA ≥50 c/mL at Week 48 by Subgroup – Snapshot Analysis	Non-inferiority margin is 4%. Adjust the footnotes, reference line and labels as appropriate. For WK96, replace 'Week 48' with 'Week 96' in title.	W48, W96
Secondary and Exploratory Efficacy Analyses							
2.3	2.3	NA	Intent-to-Treat Exposed	201585/primary_02/F2.3	Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		HL, W48, W96
2.4	2.4	NA	Intent-to-Treat Exposed	201584/primary_01/F2.4	Unadjusted Treatment Difference in Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL at Week 48 by Subgroup – Snapshot Analysis	Adjust the footnotes, reference line and labels as appropriate. For WK96, replace 'Week 48' with 'Week 96' in title.	W48, W96

Efficacy Figures							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.5	2.5	NA	Intent-to-Treat Exposed	201585/primary_02/F2.10	Proportion (95% CI) of Subjects with HIV-1 RNA >=200 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		W48, W96
2.6	2.6	NA	Intent-to-Treat Exposed	201585/primary_02/F2.5	Proportion (95% CI) of Subjects with HIV-1 RNA <200 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		W48, W96
2.7	2.7	2.1	Intent-to-Treat Exposed	207966/idmc_03/F2.1	Individual Plasma HIV-1 RNA (log10 c/mL) Profiles by Visit – for CVF subjects		HL, W48, W96, EOS
2.8	2.8	NA	Intent-to-Treat Exposed	207966/idmc_03/F2.1	Individual Plasma HIV-1 RNA (log10 c/mL) Profiles by Visit for subjects Who are in the Category of 'HIV-1 RNA >=50 c/mL' at Week 48 per Snapshot algorithm	For WK96, replace 'Week 48' with 'Week 96' in the title.	HL, W48, W96

15.14.5.4. Safety Tables

Safety Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Exposure							
3.1	3.1	3.1	Safety	201585/primary_02/T3.1	Summary of Extent of Exposure to Investigational Product (Maintenance Phase)	No need for the first two footnotes. Update the last footnote to be below: Note: The injection at nominal visit of Week 100 was not included in the summary of Exposure (No. of IP injections).	W48, W96, EOS
NA	3.2	3.2	Safety	201585/primary_02/T3.1	Summary of Extent of Exposure to Investigational Product (Maintenance + Extension Phase)	Remove the footnotes.	W96, EOS
3.2	3.3	NA	Safety	201585/primary_03/T3.102	Summary of Needle Length and Gauge for CAB Injection (Maintenance Phase)	Display both arms.	W48, W96
3.3	3.4	NA	Safety	201585/primary_03/T3.103	Summary of Needle Length and Gauge for RPV Injection (Maintenance Phase)	Display both arms.	W48, W96
3.4	3.5	NA	Safety	201585/primary_02/T3.6	Summary of Adherence to CAB/RPV Injection Dosing Schedule (Maintenance Phase)	Display both arms. Adjust the footnotes as appropriate.	W48, W96
Adverse Events							
3.5	3.6	NA	Safety	201585/primary_02/T3.7	Summary of All Adverse Events by System Organ Class (Maintenance Phase)		W48, W96
3.6	3.7	NA	Safety	201585/primary_02/T3.8	Summary of All Adverse Events by System Organ Class and Maximum Toxicity (Maintenance Phase)		HL, W48, W96

Safety Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
NA	3.8	3.3	Safety	201585/primary_02/T3.8	Summary of All Adverse Events by System Organ Class and Maximum Toxicity (Maintenance + Extension Phase)		W96, EOS
3.7	3.9	NA	Safety	201585/primary_02/T3.8	Summary of All Adverse Events Excluding Study Drug Injection Site Reactions by System Organ Class and Maximum Toxicity (Maintenance Phase)		HL, W48, W96
NA	NA	3.4	Long-term Follow-up	201585/primary_02/T3.8	Summary of All Adverse Events by System Organ Class and Maximum Toxicity (Long-term Follow-up Phase)		EOS
3.8	3.10	NA	Safety	201585/primary_02/T3.11	Summary of All On-treatment Adverse Events by System Organ Class and Maximum Toxicity (Maintenance Phase)		W48, W96
3.9	NA	NA	Oral Lead-in	201585/primary_02/T3.13	Summary of All Adverse Events by System Organ Class and Maximum Toxicity (Oral Lead-in Period during the Maintenance Phase)	Remove the footnote. Display both arms.	W48
3.10	3.11	NA	Safety	201585/primary_02/T3.14	Summary of Common Adverse Events (>=5%) by Overall Frequency (Maintenance Phase)		W48, W96
3.11	3.12	NA	Safety	201585/primary_02/T3.15	Summary of Common Grade 2-5 Adverse Events (>=1%) by Overall Frequency (Maintenance Phase)		W48, W96
3.12	3.13	NA	Safety	201585/primary_02/T3.16	Summary of All Drug-related Adverse Events by System Organ Class (Maintenance Phase)		W48, W96

Safety Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.13	3.14	NA	Safety	201585/primary_02/T3.17	Summary of All Drug-related Adverse Events by System Organ Class and Maximum Toxicity (Maintenance Phase)		HL, W48, W96
NA	3.15	3.5	Safety	201585/primary_02/T3.17	Summary of All Drug-related Adverse Events by System Organ Class and Maximum Toxicity (Maintenance + Extension Phase)		W96, EOS
3.14	3.16	NA	Safety	201585/primary_02/T3.101	Summary of All Drug-related Adverse Events Excluding Study Drug Injection Site Reactions by System Organ Class and Maximum Toxicity (Maintenance Phase)		HL, W48, W96
3.15	3.17	NA	Safety	201585/primary_02/T3.20	Summary of All Drug-Related Grade 2-5 Adverse Events by Overall Frequency (Maintenance Phase)		W48, W96
Serious and Other Significant Adverse Events							
3.16	3.18	NA	Safety	201585/primary_02/T3.21	Summary of Serious Adverse Events by System Organ Class (Maintenance Phase)		HL, W48, W96
NA	3.19	3.6	Safety	201585/primary_02/T3.21	Summary of Serious Adverse Events by System Organ Class (Maintenance + Extension Phase)		W96, EOS
3.17	3.20	3.7	Long-term Follow-up	201585/primary_02/T3.24	Summary of Serious Adverse Events by System Organ Class (Long-term Follow-up Phase)		W48, W96, EOS
3.18	NA	NA	Oral Lead-in	201585/primary_02/T3.25	Summary of Serious Adverse Events by System Organ Class (Oral Lead-in Period during the Maintenance Phase)	Display both arms.	W48

Safety Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.19	3.21	NA	Safety	201585/primary_02/T3.26	Summary of Drug-related Serious Adverse Events by System Organ Class (Maintenance Phase)		W48, W96
NA	3.22	3.8	Safety	201585/primary_02/T3.26	Summary of Drug-related Serious Adverse Events by System Organ Class (Maintenance + Extension Phase)		W96, EOS
3.20	3.23	NA	Safety	201585/primary_02/T3.29	Summary of Non-Fatal Serious Adverse Events by Overall Frequency (Maintenance Phase)		W48, W96
3.21	3.24	NA	Safety	201585/primary_02/T3.30	Summary of Drug-related Non-Fatal Serious Adverse Events by Overall Frequency (Maintenance Phase)		W48, W96
3.22	3.25	NA	Safety	201585/primary_02/T3.31	Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by System Organ Class (Maintenance Phase)		HL, W48, W96
NA	3.26	3.9	Safety	201585/primary_02/T3.31	Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by System Organ Class (Maintenance + Extension Phase)		W96, EOS
3.23	NA	NA	Oral Lead-in	201585/primary_02/T3.34	Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by System Organ Class (Oral Lead-in Period during the Maintenance Phase)	Remove the footnote. Display both arms.	W48
3.24	3.27	NA	Safety	201585/primary_02/T3.35	Summary of Common (>=5%) Non-Serious Adverse Events (Maintenance Phase)		W48, W96

Safety Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.25	3.28	NA	Safety	201585/primary_02/T3.36	Summary of Subjects and Number of Occurrences of Common (>=5%) Non-Serious Adverse Events by System Organ Class (Maintenance Phase)		W48, W96
3.26	3.29	NA	Safety	201585/primary_02/T3.37	Summary of Subjects and Number of occurrences of SAEs, Fatal SAEs, and Drug-related SAEs (Maintenance Phase)		W48, W96
3.27	3.30	NA	Safety	201585/primary_02/T3.38	Summary of Cumulative Adverse Events by Visit (Maintenance Phase)	Note that this table only display AEs occurring >=5% subjects during Maintenance Phase.	W48, W96
Study Drug Injection Site Reaction Adverse Events (display for both arms)							
3.28	3.31	NA	Safety	201585/primary_02/T3.40	Summary of Study Drug Injection Site Reaction Adverse Events (Event-level Summary) - Maintenance Phase		HL, W48, W96
NA	3.32	3.10	Safety	201585/primary_02/T3.40	Summary of Study Drug Injection Site Reaction Adverse Events (Event-level Summary) - Maintenance + Extension Phase		W96, EOS
3.29	3.33	NA	Safety	201585/primary_02/T3.43	Summary of Subject-level Characteristics of Study Drug Injection Site Reaction Adverse Events – Overall and Common (Maintenance Phase)		W48, W96
NA	3.34	3.11	Safety	201585/primary_02/T3.43	Summary of Subject-level Characteristics of Study Drug Injection Site Reaction Adverse Events – Overall and Common (Maintenance + Extension Phase)		W96, EOS

Safety Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.30	3.35	NA	Safety	201585/primary_02/T3.46	Summary of Study Drug Injection Site Reaction Adverse Events by Visit and Maximum Severity – Overall and Common (Maintenance Phase)	Change the second footnote to 'Note: Common ISR includes pain, induration, nodules and any other ISR with >=5% subjects in either treatment arm.' Footnote may be adjusted for clarifications.	W48, W96
3.31	3.36	NA	Safety	201585/primary_02/T3.47	Summary of Drug-related Study Drug Injection Site Reaction Adverse Events (Event-level Summary) - CAB (Maintenance Phase)		W48, W96
3.32	3.37	NA	Safety	201585/primary_02/T3.48	Summary of Drug-related Subject-level Characteristics of Study Drug Injection Site Reaction Adverse Events (Maintenance Phase) - Overall and Common (CAB)		W48, W96
3.33	3.38	NA	Safety	201585/primary_02/T3.49	Summary of Overall and Common Drug-related Study Drug Injection Site Reaction Adverse Events by Visit and Maximum Severity (Maintenance Phase) - CAB	Footnote may be adjusted for clarifications.	W48, W96
3.34	3.39	NA	Safety	201585/primary_02/T3.50	Summary of Maximum Drug-related Study Drug Injection Site Reaction Adverse Event Grade by Needle Length (Maintenance Phase) – Common (CAB)	Update the needle length in column header to be "<=1.5 inches', '>1.5 to <2 inches' and '>=2 inches' respectively. Change the first footnote to 'Note: Common ISR includes pain, induration, nodules and any other ISR with >=5% subjects in either treatment arm.'. Remove the second footnote.	W48, W96

Safety Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.35	3.40	NA	Safety	201585/primary_02/T3.51	Summary of Drug-related Study Drug Injection Site Reaction Adverse Events (Event-level Summary) - RPV (Maintenance Phase)		W48, W96
3.36	3.41	NA	Safety	201585/primary_02/T3.52	Summary of Drug-related Subject-level Characteristics of Study Drug Injection Site Reaction Adverse Events (Maintenance Phase) - Overall and Common (RPV)		W48, W96
3.37	3.42	NA	Safety	201585/primary_02/T3.53	Summary of Overall and Common Drug-related Study Drug Injection Site Reaction Adverse Events by Visit and Maximum Severity (Maintenance Phase) - RPV	Footnote may be adjusted for clarifications.	W48, W96
3.38	3.43	NA	Safety	201585/primary_02/T3.54	Summary of Maximum Drug-related Study Drug Injection Site Reaction Adverse Event Grade by Needle Length (Maintenance Phase) – Common (RPV)	Update the needle length in column header to be "<=1.5 inches', '>1.5 to < 2 inches' and '>=2 inches' respectively. Change the first footnote to 'Note: Common ISR includes pain, induration, nodules and any other ISR with >=5% subjects in either treatment arm.'. Remove the second footnote.	W48, W96
Laboratory: Chemistry and Hematology							
3.39	3.44	3.12	Safety	201585/primary_02/T3.55	Summary of Chemistry Changes from Baseline by Visit (Maintenance + Extension Phase)	Present GFR, lipids and glucose in both conventional and standard units. Change 'Post Baseline' to 'Post-baseline' in the footnote.	W48, W96, EOS
3.40	3.45	3.13	Safety	201585/primary_02/T3.59	Summary of Chemistry Values by Visit (Maintenance + Extension Phase)	Present GFR, lipids and glucose in both conventional and standard units. Change 'Post Baseline' to 'Post-'	W48, W96, EOS

Safety Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
						baseline' in the footnote.	
3.41	3.46	3.14	Safety	201585/primary_02/T3.60	Summary of Hematology Changes from Baseline by Visit (Maintenance + Extension Phase)	Change 'Post Baseline' to 'Post-baseline' in the footnote.	W48, W96, EOS
3.42	3.47	3.15	Safety	201585/primary_02/T3.59	Summary of Hematology Values by Visit (Maintenance + Extension Phase)	Remove the first footnote. Change 'Post Baseline' to 'Post-baseline' in the footnote.	W48, W96, EOS
3.43	3.48	NA	Safety	201585/primary_02/T3.61	Summary of Maximum Post-Baseline Emergent Chemistry Toxicities (Maintenance Phase)	Add "Emergent is relative to last toxicity up to and including baseline." to the end of the second footnote.	W48, W96
NA	3.49	3.16	Safety	201585/primary_02/T3.61	Summary of Maximum Post-Baseline Emergent Chemistry Toxicities (Maintenance + Extension Phase)	Adjust the footnote similar to above.	W96, EOS
3.44	NA	NA	Oral Lead-in	201585/primary_02/T3.64	Summary of Maximum Post-Baseline Emergent Chemistry Toxicities - Oral Lead-in Period during the Maintenance Phase	Display both arms. Adjust the footnote similarly to above.	W48
3.45	3.50	NA	Safety	201585/primary_02/T3.65	Summary of Maximum Post-Baseline Emergent Hematology Toxicities (Maintenance Phase)	Adjust the footnote similarly to above.	W48, W96
NA	3.51	3.17	Safety	201585/primary_02/T3.65	Summary of Maximum Post-Baseline Emergent Hematology Toxicities (Maintenance + Extension Phase)	Adjust the footnote similarly to above.	W96, EOS
3.46	NA	NA	Oral Lead-in	201585/primary_02/T3.68	Summary of Maximum Post-Baseline Emergent Hematology Toxicities - Oral Lead-in Period during the Maintenance Phase	Display both arms. Adjust the footnote similarly to above.	W48

Safety Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Laboratory: Urinalysis							
3.47	3.52	3.18	Safety	201585/primary_02/T3.69	Summary of Urinalysis Dipstick Results by Visit (Maintenance + Extension Phase)	Change 'Post Baseline' to 'Post-Baseline' in the footnote.	W48, W96, EOS
3.48	3.53	3.19	Safety	201585/primary_02/T3.70	Summary of Urine Concentrations Changes from Baseline by Visit (Maintenance + Extension Phase)	Change 'Post Baseline' to 'Post-Baseline' in the footnote.	W48, W96, EOS
3.49	3.54	NA	Safety	201585/primary_02/T3.71	Summary of Changes in Proteinuria Baseline Laboratory Result to Maximum Post-Baseline Laboratory Result (Maintenance Phase)	Change 'Post Baseline' to 'Post-Baseline' in the footnote.	W48, W96
Laboratory: Lipid							
3.50	3.55	NA	Safety	201585/primary_02/T3.72	Summary of Changes in Baseline NCEP Fasting Lipid Category to Maximum Post-Baseline Category – Triglycerides (Maintenance Phase)		W48, W96
3.51	3.56	NA	Safety	201585/primary_02/T3.73	Summary of Changes in Baseline NCEP Fasting Lipid Category to Maximum Post-Baseline Category – Total Cholesterol (Maintenance Phase)		W48, W96
3.52	3.57	NA	Safety	201585/primary_02/T3.74	Summary of Changes in Baseline NCEP Fasting Lipid Category to Minimum Post-Baseline Category – HDL Cholesterol (Maintenance Phase)		W48, W96
3.53	3.58	NA	Safety	201585/primary_02/T3.75	Summary of Changes in Baseline NCEP Fasting Lipid Category to Maximum Post-Baseline Category – LDL Cholesterol (Maintenance Phase)		W48, W96

Safety Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.54	3.59	NA	Safety	201585/primary_02/T3.58	Summary of Fasting Lipids Percentage Changes from Baseline by Visit (Maintenance Phase) - Lipids LOCF	Change 'Post Baseline' to 'Post-Baseline' in the footnote.	W48, W96
3.55	3.60	NA	Safety	201585/primary_02/T3.76	Summary of Fasting TC/HDL ratio Changes from Baseline (Maintenance Phase) – Lipids LOCF	Change 'Post Baseline' to 'Post-Baseline' in the footnote.	W48, W96
Laboratory: Hepatobiliary (Liver)							
3.56	3.61	NA	Safety	201585/primary_02/T3.80	Summary of Liver Monitoring/Stopping Event Reporting (Maintenance Phase)		W48, W96
3.57	3.62	NA	Safety	201585/primary_02/T3.81	Summary of Subjects Meeting Hepatobiliary Abnormality Criteria (Maintenance Phase)		W48, W96
NA	3.63	3.20	Safety	201585/primary_02/T3.81	Summary of Subjects Meeting Hepatobiliary Abnormality Criteria (Maintenance +Extension Phase)		W96, EOS
3.58	NA	NA	Oral Lead-in	201585/primary_02/T3.84	Summary of Subjects Meeting Hepatobiliary Abnormality Criteria – Oral Lead-in Period during the Maintenance Phase	Display both arms.	W48
ECG							
3.59	3.64	3.21	Safety	201585/primary_02/T3.85	Summary of ECG Findings (Maintenance + Extension Phase)	Change 'Post Baseline' to 'Post-Baseline' in the footnote.	W48, W96, EOS
3.60	3.65	3.22	Safety	201585/primary_02/T3.88	Summary of Change from Baseline in ECG values by Visit (Maintenance + Extension Phase)	Change 'Post Baseline' to 'Post-Baseline' in the footnote.	W48, W96, EOS
3.61	3.66	3.23	Safety	201585/primary_02/T3.91	Summary of QTc Values by Category (Maintenance + Extension Phase)	Change 'Post Baseline' to 'Post-Baseline' in the footnote.	W48, W96, EOS

Safety Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.62	3.67	3.24	Safety	201585/primary_02/T3.94	Summary of Change from Baseline QTc Values by Category (Maintenance + Extension Phase)	Change 'Post Baseline' to 'Post-Baseline' in the footnote.	W48, W96, EOS
Vital Signs and eC-SSRS							
3.63	3.68	NA	Safety	201585/primary_02/T3.97	Summary of Change from Baseline in Vital Signs by Visit (Maintenance Phase)	Change 'Post Baseline' to 'Post-Baseline' in the footnote.	W48, W96
3.64	3.69	NA	Safety	SAFE_T1	Summary of BMI Shift from Baseline by Visit (Maintenance Phase)		W48, W96
3.65	3.70	NA	Safety	201585/primary_02/T3.99	Summary of Subjects with eC-SSRS Suicidal Ideation or Behaviour (Maintenance Phase)	Change 'post baseline' to 'post-baseline' in the row header.	W48, W96
Adverse Event of Special Interest (AESI)							
3.66	3.71	NA	Safety	201585/primary_02/T3.100	Summary of Depression, Anxiety and Suicidal Ideation/Behaviour Adverse Events by System Organ Class, Maximum DAIDS Toxicity Grade, and Prior History of Depression, Anxiety and Suicidal Ideation at Screening (Maintenance Phase)		W48, W96
3.67-3.83	3.72-3.88	NA	Safety	209522/iss_01/T3.38-3.49, T3.51-3.55	Summary of XXX Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrence) – Maintenance Phase	Only display data from this study, no need for showing study number. For 'XXX', refer to Table 4.	W48, W96
3.84	3.89	NA	Safety	209522/iss_01/T3.62	Summary of Characteristics of Common Adverse Events of Special Interest – Maintenance Phase	Only display data from this study, no need for showing study number. Present by individual common AESI.	W48, W96

15.14.5.5. Safety Figures

Note: Unless otherwise specified, display both arms.

Safety Figures							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.1	3.1	NA	Safety	201585/primary_02/F3.1	Plot of Common Adverse Events and Relative Risk - Q8W vs. Q4W (Maintenance Phase) – Excluding Study Drug ISRs	Remove the second footnote.	HL, W48, W96
3.2	3.2	NA	Safety	201585/primary_02/F3.1	Plot of Common Study Drug Injection Site Reaction Adverse Events and Relative Risk - Q8W vs. Q4W (Maintenance Phase)	Remove the second footnote.	HL, W48, W96
3.3	3.3	NA	Safety	201585/primary_02/F3.5	Plot of Onset, Duration, and Severity of Overall and Common Study Drug Injection Site Reaction AEs by Maximum Grade — CAB and/or RPV (Maintenance Phase)		W48, W96
3.4	3.4	NA	Safety	201585/primary_02/F3.6	Plot of Onset, Duration, and Severity of Overall and Common Drug-related Study Drug Injection Site Reaction AEs by Maximum Grade — CAB (Maintenance Phase)		W48, W96
3.5	3.5	NA	Safety	201585/primary_02/F3.7	Plot of Onset, Duration, and Severity of Overall and Common Drug-related Study Drug Injection Site Reaction AEs by Maximum Grade — RPV (Maintenance Phase)		W48, W96
3.6	3.6	NA	Safety	201585/primary_02/F3.8	Plot of Incidence of Maintenance Phase Study Drug Injection Site Reaction Adverse Events by Visit (Overall and Common) – CAB and/or RPV	Footnote may be adjusted for clarifications.	W48, W96
3.7	3.7	NA	Safety	201585/primary_02/F3.9	Plot of Incidence of Maintenance Phase Drug-Related Study Drug Injection Site Reaction Adverse Events by Visit (Overall and Common) – CAB	Footnote may be adjusted for clarifications.	W48, W96

Safety Figures							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.8	3.8	NA	Safety	201585/primary_02/F3.10	Plot of Incidence of Maintenance Phase Drug-Related Study Drug Injection Site Reaction Adverse Events by Visit (Overall and Common) – RPV	Footnote may be adjusted for clarifications.	W48, W96
3.9	3.9	NA	Safety	201585/primary_02/F3.11	Plot of Incidence of Grade 3-5 Maintenance Phase Study Drug Injection Site Reaction Adverse Events by Visit (Overall and Common) - CAB and/or RPV	Footnote may be adjusted for clarifications.	W48, W96
3.10	3.10	NA	Safety	201585/primary_02/F3.12	Plot of Incidence of Grade 3-5 Maintenance Phase Drug-related Study Drug Injection Site Reaction Adverse Events by Visit (Overall and Common) - CAB	Footnote may be adjusted for clarifications.	W48, W96
3.11	3.11	NA	Safety	201585/primary_02/F3.13	Plot of Incidence of Grade 3-5 Maintenance Phase Drug-related Study Drug Injection Site Reaction Adverse Events by Visit (Overall and Common) - RPV	Footnote may be adjusted for clarifications.	W48, W96
3.12	3.12	NA	Safety	201585/primary_02/F3.2	Scatter Plot of Maximum vs. Baseline for ALT (Maintenance Phase)	Display at log10 scale.	HL, W48, W96
3.13	3.13	NA	Safety	201585/primary_02/F3.3	Scatter Plot of Maximum ALT vs. Maximum Total Bilirubin (Maintenance Phase)		HL, W48, W96
3.14	3.14	NA	Safety	201585/primary_02/F3.4	Matrix Plot of Maximum Liver Chemistries during the Maintenance Phase		HL, W48, W96
3.15	3.15	NA	Safety	201585/primary_02/F3.14	Bar Chart of Lipid NCEP Categories at Week 48 vs. Baseline – Triglycerides, Total Cholesterol, LDL Cholesterol	For WK96, replace ‘Week 48’ with ‘Week 96’ in the title.	W48, W96
3.16	3.16	NA	Safety	201585/primary_02/F3.15	Bar Chart of Lipid NCEP Categories at Week 48 vs. Baseline - HDL Cholesterol	For WK96, replace ‘Week 48’ with ‘Week 96’ in the title.	W48, W96

Safety Figures							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.17	3.17	NA	Safety	SAFE_F1	Histogram of Timeliness of Injections (Maintenance Phase)		W48, W96

15.14.5.6. Pharmacokinetic Tables

Note: For WK48 deliverable, data from visits up to Week 48 are included.

Pharmacokinetic Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
4.1	4.1	NA	Pharmacokinetic	201585/primary_02/T4.1	Summary of Plasma CAB PK Concentration (ug/mL) -Time Data by Treatment and Visit – Including Log-transformed Statistics	Remove the first footnote.	W48, W96
4.2	4.2	NA	Pharmacokinetic	201585/primary_02/T4.2	Summary of Plasma RPV PK Concentration (ng/mL) -Time Data by Treatment and Visit – Including Log-transformed Statistics	Remove the first footnote.	W48, W96
4.3	4.3	NA	Pharmacokinetic	201585/primary_02/T4.3	Summary of Evaluable Plasma CAB PK Concentration (ug/mL) -Time Data by Treatment and Visit – Including Log-transformed Statistics	Remove the first footnote.	W48, W96
4.4	4.4	NA	Pharmacokinetic	201585/primary_02/T4.4	Summary of Evaluable Plasma RPV PK Concentration (ng/mL) -Time Data by Treatment and Visit – Including Log-transformed Statistics	Remove the first footnote.	W48, W96
4.5	4.5	NA	Pharmacokinetic	201585/primary_02/T4.3	Summary of Evaluable Plasma CAB PK Concentration (ug/mL) -Time Data by Strata and Treatment and Visit – Including Log-transformed Statistics	Display by rederived randomization strata and add footnote for strata.	W48, W96
4.6	4.6	NA	Pharmacokinetic	201585/primary_02/T4.4	Summary of Evaluable Plasma RPV PK Concentration (ng/mL) -Time Data by Strata and Treatment and Visit – Including Log-transformed Statistics	Display by rederived randomization strata and add footnote for strata.	W48, W96
4.7	4.7	NA	Pharmacokinetic	201585/primary_02/T4.6	Summary of Results of Steady State Assessment by Strata for Q8W Arm- Evaluable Concentration	Display by rederived randomization strata and add footnote for strata. For Q8W arm only.	W48

15.14.5.7. Pharmacokinetic Figures

Note: Unless otherwise specified, display both arms.

Pharmacokinetic Figures							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
4.1	4.1	NA	Pharmacokinetic	201585/primary_02/ F4.1	Individual Plasma CAB Concentration-Time Plots (Linear and Semi-Log)	Also include prior exposure to CAB+RPV (e.g. 0, 1-24, >24 weeks) for each subject.	W48, W96
4.2	4.2	NA	Pharmacokinetic	201585/primary_02/ F4.2	Individual Plasma RPV Concentration-Time Plots (Linear and Semi-Log)	Also include prior exposure to CAB+RPV (e.g. 0, 1-24, >24 weeks) for each subject.	W48, W96
4.3	4.3	NA	Pharmacokinetic	201585/primary_02/ F4.3	Mean (SD) Plasma CAB Concentration-Time Plots (Linear and Semi-Log)	For WK48, data from visits up to Week 48 are included.	W48, W96
4.4	4.4	NA	Pharmacokinetic	201585/primary_02/ F4.5	Mean (SD) Plasma RPV Concentration-Time Plots (Linear and Semi-Log)	For WK48, data from visits up to Week 48 are included.	W48, W96
4.5	4.5	NA	Pharmacokinetic	201585/primary_02/ F4.7	Mean (SD) Evaluable Plasma CAB Concentration-Time Plots (Linear and Semi-Log)	For WK48, data from visits up to Week 48 are included.	W48, W96
4.6	4.6	NA	Pharmacokinetic	201585/primary_02/ F4.9	Mean (SD) Evaluable Plasma RPV Concentration-Time Plots (Linear and Semi-Log)	For WK48, data from visits up to Week 48 are included.	W48, W96
4.7	4.7	NA	Pharmacokinetic	201585/primary_02/ F4.7	Mean (SD) Evaluable Plasma CAB Concentration-Time Plots by Strata (Linear and Semi-Log)	Display by rederived randomization strata and add footnote for strata. For WK48, data from visits up to Week 48 are included.	W48, W96

Pharmacokinetic Figures							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
4.8	4.8	NA	Pharmacokinetic	201585/primary_02/ F4.9	Mean (SD) Evaluable Plasma RPV Concentration-Time Plots by Strata (Linear and Semi-Log)	Display by rederived randomization strata and add footnote for strata. For WK48, data from visits up to Week 48 are included.	W48, W96
4.9	4.9	NA	Pharmacokinetic	201585/primary_02/ F4.4	Median (5th and 95th Percentile) Plasma CAB Concentration-Time Plots (Linear and Semi-Log)	For WK48, data from visits up to Week 48 are included.	W48, W96
4.10	4.10	NA	Pharmacokinetic	201585/primary_02/ F4.6	Median (5th and 95th Percentile) Plasma RPV Concentration-Time Plots (Linear and Semi-Log)	For WK48, data from visits up to Week 48 are included.	W48, W96
4.11	4.11	NA	Pharmacokinetic	201585/primary_02/ F4.8	Median (5th and 95th Percentile) Evaluable Plasma CAB Concentration-Time Plots (Linear and Semi-Log)	For WK48, data from visits up to Week 48 are included.	W48, W96
4.12	4.12	NA	Pharmacokinetic	201585/primary_02/ F4.10	Median (5th and 95th Percentile) Evaluable Plasma RPV Concentration-Time Plots (Linear and Semi-Log)	For WK48, data from visits up to Week 48 are included.	W48, W96
4.13	4.13	NA	Pharmacokinetic	201585/primary_02/ F4.8	Median (5th and 95th Percentile) Evaluable Plasma CAB Concentration-Time Plots by Strata (Linear and Semi-Log)	Display by rederived randomization strata and add footnote for strata. For WK48, data from visits up to Week 48 are included.	W48, W96
4.14	4.14	NA	Pharmacokinetic	201585/primary_02/ F4.10	Median (5th and 95th Percentile) Evaluable Plasma RPV Concentration-Time Plots by Strata (Linear and Semi-Log)	Display by rederived randomization strata and add footnote for strata. For WK48, data from visits up to Week 48 are included.	W48, W96

15.14.5.8. Pharmacokinetic / Pharmacodynamic Tables

Note: Unless otherwise specified, display by treatment arm.

Pharmacokinetic / Pharmacodynamic Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
PK / PD Efficacy							
5.1	5.1	NA	Pharmacokinetic	201584/primary_01/T5.1	Univariable Logistic Regression Analysis of Snapshot 'HIV-1 RNA ≥50 c/mL' at Week 48 by Trough PK Concentration and Subgroup for Subjects without Prior Exposure to CAB + RPV	For WK96, replace 'Week 48' with 'Week 96' in title. Do not display by treatment arm.	W48, W96
5.2	5.2	NA	Pharmacokinetic	201584/primary_01/T5.2	Multivariable Logistic Regression Analysis of Predictors of Snapshot 'HIV-1 RNA ≥50 c/mL' at Week 48 for Subjects without Prior Exposure to CAB + RPV	For WK96, replace 'Week 48' with 'Week 96' in title. Adjust the footnote as appropriate. Do not display by treatment arm.	W48, W96
5.3	5.3	NA	Pharmacokinetic	201584/primary_01/T5.5	Summary of Week 8 Trough CAB PK concentration by Snapshot 'HIV-1 RNA ≥50 c/mL' (Yes vs. No) at Week 48 for Subjects without Prior Exposure to CAB + RPV – Including Log-transformed Statistics	For WK96, replace 'Week 48' with 'Week 96' in title.	W48, W96
5.4	5.4	NA	Pharmacokinetic	201584/primary_01/T5.6	Summary of Week 8 Trough RPV PK concentration by Snapshot 'HIV-1 RNA ≥50 c/mL' (Yes vs. No) at Week 48 for Subjects without Prior Exposure to CAB + RPV – Including Log-transformed Statistics	For WK96, replace 'Week 48' with 'Week 96' in title.	W48, W96

15.14.5.9. Pharmacokinetic / Pharmacodynamic Figures

Pharmacokinetic / Pharmacodynamic Figures							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
PK / PD Efficacy Analyses							
5.1	5.1	NA	Pharmacokinetic	201585/primary_02/F5.3	Scatter Plot of Week 8 Trough CAB PK Concentration by Snapshot 'HIV-1 RNA ≥50 c/mL' (Yes vs. No) at Week 48 for Subjects without Prior Exposure to CAB + RPV	For WK96, replace 'Week 48' with 'Week 96' in title. Display by treatment arm.	W48, W96
5.2	5.2	NA	Pharmacokinetic	201585/primary_02/F5.4	Scatter Plot of Week 8 Trough RPV PK Concentration by Snapshot 'HIV-1 RNA ≥50 c/mL' (Yes vs. No) at Week 48 for Subjects without Prior Exposure to CAB + RPV	For WK96, replace 'Week 48' with 'Week 96' in title. Display by treatment arm.	W48, W96
5.3	5.3	NA	Pharmacokinetic	201585/primary_02/F5.7	Individual CAB Trough Concentration-time Profiles for Subjects with Snapshot 'HIV-1 RNA ≥50 c/mL' at Week 48 and Median, 5th & 95th Percentile of CAB Conc-Time Profiles for Other Subjects (Semi-Log)	For WK96, replace 'Week 48' with 'Week 96' in title. Display by treatment arm.	W48, W96
5.4	5.4	NA	Pharmacokinetic	201585/primary_02/F5.8	Individual RPV Trough Concentration-time Profiles for Subjects with Snapshot 'HIV-1 RNA ≥50 c/mL' at Week 48 and Median, 5th & 95th Percentile of RPV Conc-Time Profiles for Other Subjects (Semi-Log)	For WK96, replace 'Week 48' with 'Week 96' in title. Display by treatment arm.	W48, W96
5.5	5.5	NA	Pharmacokinetic	201585/primary_02/F5.10	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 for Subjects without Prior Exposure to CAB + RPV	For WK96, replace 'Week 48' with 'Week 96' in title. Display by treatment arm.	W48, W96

Pharmacokinetic / Pharmacodynamic Figures							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
PK / PD Safety Analyses							
5.6	5.6	NA	Pharmacokinetic	201585/primary_ 02/F5.13	Scatter Plot of Maximum Change from Baseline in ALT versus Last Trough CAB PK Concentrations by Strata and Treatment during the Maintenance Phase	Display by strata and treatment arm. Add footnote for rederived randomization strata.	W48, W96
5.7	5.7	NA	Pharmacokinetic	201585/primary_ 02/F5.14	Scatter Plot of Maximum Change from Baseline in ALT versus Last Trough RPV PK Concentrations by Strata and Treatment during the Maintenance Phase	Display by strata and treatment arm. Add footnote for rederived randomization strata.	W48, W96
5.8	5.8	NA	Pharmacokinetic	201585/primary_ 02/F5.15	Scatter Plot of Maximum Change from Baseline in Total Bilirubin versus Last Trough CAB PK Concentrations by Strata and Treatment during the Maintenance Phase	Display by strata and treatment arm. Add footnote for rederived randomization strata.	W48, W96
5.9	5.9	NA	Pharmacokinetic	201585/primary_ 02/F5.16	Scatter Plot of Maximum Change from Baseline in Total Bilirubin versus Last Trough RPV PK Concentrations by Strata and Treatment during the Maintenance Phase	Display by strata and treatment arm. Add footnote for rederived randomization strata.	W48, W96
5.10	5.10	NA	Pharmacokinetic	201585/primary_ 02/F5.17	Box Plot of Maximum Toxicity Grades of Most Frequently Reported Study Drug ISR Adverse Events versus Last Trough CAB PK Concentrations during the Maintenance Phase by Strata and Treatment	Display by strata and treatment arm. Add footnote for rederived randomization strata. Adjust the footnotes as appropriate.	W48, W96

Pharmacokinetic / Pharmacodynamic Figures							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
5.11	5.11	NA	Pharmacokinetic	201585/primary_02/F5.18	Box Plot of Maximum Toxicity Grades of Most Frequently Reported Study Drug ISR Adverse Events versus Last Trough RPV PK Concentrations during the Maintenance Phase by Strata and Treatment	Display by treatment arm. Adjust the footnotes as appropriate.	W48, W96

15.14.5.10. Health Outcomes Tables

Health Outcomes Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Perception of Injection (PIN)							
6.1	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.1	Proportion of Subjects with Each Individual Item Score in PIN by Visit –LOCF (Maintenance Phase)	Display both arms.	W48
6.2	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.2	Summary of PIN in Domain Scores (CCI [redacted], and CCI [redacted]) and Individual Items Scores (CCI [redacted]) by Visit (Maintenance Phase)	Display both arms.	W48
6.3	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.3	Summary and Statistical Analysis of PIN in Domain Scores (CCI [redacted], and CCI [redacted]) and Individual Items Scores (CCI [redacted]) by Visit - LOCF (Maintenance Phase)	Display both arms. Adjust the first half of the footnote to "[1] Week 24/48 was compared with the 1st visit (Week 8) based on Wilcoxon signed-rank test, respectively."	W48
6.4	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.4	Summary of PIN Change from Week 8 in Domain Scores (CCI [redacted], and CCI [redacted]) and Individual Items Scores (CCI [redacted]) by Visit (Maintenance Phase)	Display both arms. Adjust the footnote to "Note: Actual values are shown at Week 8."	W48

Health Outcomes Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
6.5	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.5	Summary of PIN Change from Week 8 in Domain Scores (CCI [redacted] and CCI [redacted]) and Individual Items Scores (CCI [redacted] CCI [redacted]) by Visit – LOCF (Maintenance Phase)	Display both arms. Adjust the footnote to "Note: Actual values are shown at Week 8."	W48
6.6	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.11	Statistical Analysis of PIN Change from Week 8 in Domain Scores (CCI [redacted] CCI [redacted] and CCI [redacted]) and Individual Items Scores (CCI [redacted] CCI [redacted]) by Visit – LOCF (Maintenance Phase)	Adjust the column header and the footnote as appropriate.	W48
Health-related Quality of Life (HAT-QoL)							
6.7	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.6	Proportion of Subjects with Each Individual Questionnaire Item Score in HAT-QoL by Visit - LOCF (Maintenance Phase)		W48
6.8	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.7	Summary of Quality of Life (HAT-QoL) Score in Life Satisfaction, HIV Medication, and Disclosure worries by Visit (Maintenance phase)		W48
6.9	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.8	Summary of Quality of Life (HAT-QoL) Score in Life Satisfaction, HIV Medication, and Disclosure worries by Visit - LOCF (Maintenance phase)		W48
6.10	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.9	Summary of Quality of Life Score (HAT-QoL)- Change from Baseline in Life Satisfaction, HIV Medication, and Disclosure Worries by Prior Exposure to CAB+RPV (0 vs. >=1 Weeks) and Visit (Maintenance Phase)		W48

Health Outcomes Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
6.11	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.10	Summary of Quality of Life Score (HAT-QoL)- Change from Baseline in Life Satisfaction, HIV Medication, and Disclosure Worries by Prior Exposure to CAB+RPV (0 vs. >=1 Weeks) and Visit – LOCF (Maintenance Phase)		W48
6.12	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.11	Statistical Analysis of Quality of Life Score (HAT-QoL)- Change from Baseline in Life Satisfaction, HIV Medication, and Disclosure Worries by Visit for Subjects without Prior Exposure to CAB+RPV – LOCF (Maintenance Phase)	Adjust the column header and the footnote as appropriate.	W48
6.13	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.11	Statistical Analysis of Quality of Life Score (HAT-QoL)- Change from Baseline in Life Satisfaction, HIV Medication, and Disclosure Worries by Visit for Subjects with Prior Exposure to CAB+RPV – LOCF (Maintenance Phase)	Adjust the column header and the footnote as appropriate.	W48
HIV Treatment Satisfaction Questionnaire Status Version (HIVTSQs)							
6.14	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.18	Proportion of Subjects with HIVTSQs - Individual Item Scores by Visit - LOCF (Maintenance Phase)		W48
6.15	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.19	Proportion of Subjects with HIVTSQs - Individual Item Scores by Visit and Subgroup - LOCF (Maintenance Phase)	The subgroup includes: prior exposure to CAB+RPV (0, 1-24, >=24 weeks), sex at birth, age (<35, 35 - <50, >=50), race (white, non-white), Baseline CD4+ cell count (<350, 350 – <500, >=500)	W48

Health Outcomes Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
6.16	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.20	Summary of HIVTSQs - Total Treatment Satisfaction Score by Visit (Maintenance Phase)		W48
6.17	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.21	Summary of HIVTSQs - Total Treatment Satisfaction Score by Visit – LOCF (Maintenance Phase)		W48
6.18	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.22	Summary of HIVTSQs - Change from Baseline in Total Treatment Satisfaction Score by Prior Exposure to CAB+RPV (0 vs. >=1 Weeks) and Visit (Maintenance Phase)		W48
6.19	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.23	Summary of HIVTSQs - Change from Baseline in Total Treatment Satisfaction Score by Prior Exposure to CAB+RPV (0 vs. >=1 Weeks) and Visit – LOCF (Maintenance Phase)		W48
6.20	NA	NA	Intent-to-Treat Exposed	201585/primary_03/T7.41	Summary of HIVTSQs - Change from Baseline in Individual Item Score by Prior Exposure to CAB+RPV (0 vs. >=1 Weeks) and Visit – LOCF (Maintenance Phase)		W48
6.21	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.24	Statistical Analysis of HIVTSQs - Change from Baseline in Total Treatment Satisfaction Score by Visit for Subjects without Prior Exposure to CAB+RPV - LOCF (Maintenance Phase)	Adjust column header and footnote as appropriate.	W48
6.22	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.24	Statistical Analysis of HIVTSQs - Change from Baseline in Total Treatment Satisfaction Score by Visit for Subjects with Prior Exposure to CAB+RPV - LOCF (Maintenance Phase)	Adjust column header and footnote as appropriate.	W48

Health Outcomes Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
HIV Treatment Satisfaction Questionnaire Change Version (HIVTSQc)							
6.23	NA	NA	Q4W ATLAS	201584/primary_01/T6.25	Proportion of Subjects with HIVTSQc - Individual Item Change Score at Week 48 (Maintenance Phase) for Subjects from Q4W ATLAS		W48
6.24	NA	NA	SOC	201584/primary_01/T6.25	Proportion of Subjects with HIVTSQc - Individual Item Change Score at Week 48 (Maintenance Phase) for Subjects from SOC		W48
6.25	NA	NA	Q4W ATLAS	201584/primary_01/T6.26	Summary of HIVTSQc – Total Treatment Satisfaction Change Score at Week 48 (Maintenance Phase) for Subjects from Q4W ATLAS		W48
6.26	NA	NA	SOC	201584/primary_01/T6.26	Summary of HIVTSQc – Total Treatment Satisfaction Change Score at Week 48 (Maintenance Phase) for Subjects from SOC		W48
6.27	NA	NA	Q4W ATLAS	201584/primary_02/T6.41	Summary of HIVTSQc – Individual Item Change Score at Week 48 (Maintenance Phase) for Subjects from Q4W ATLAS		W48
6.28	NA	NA	SOC	201584/primary_02/T6.41	Summary of HIVTSQc – Individual Item Change Score at Week 48 (Maintenance Phase) for Subjects from SOC		W48
6.29	NA	NA	Q4W ATLAS	201584/primary_01/T6.27	Statistical Analysis of HIVTSQc – Total Treatment Satisfaction Change Score at Week 48 for Subjects from Q4W ATLAS	Adjust column header and footnote as appropriate.	W48
6.30	NA	NA	SOC	201584/primary_01/T6.27	Statistical Analysis of HIVTSQc – Total Treatment Satisfaction Change Score at Week 48 for Subjects from SOC	Adjust column header and footnote as appropriate.	W48

Health Outcomes Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Treatment Acceptance (ACCEPT)							
6.31	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.28	Proportion of Subjects with ACCEPT - Individual Item Score by Visit - LOCF (Maintenance Phase)		W48
6.32	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.29	Summary of Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit (Maintenance Phase)		W48
6.33	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.30	Summary of Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit - LOCF (Maintenance Phase)		W48
6.34	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.31	Summary of Change from Baseline in Acceptance/General Dimension Score (ACCEPT Questionnaire) by Prior Exposure to CAB+RPV (0 vs. >=1 Weeks) and Visit (Maintenance Phase)		W48
6.35	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.32	Summary of Change from Baseline in Acceptance/General Dimension Score (ACCEPT Questionnaire) by Prior Exposure to CAB+RPV (0 vs. >=1 Weeks) and Visit - LOCF (Maintenance Phase)		W48
6.36	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.33	Statistical Analysis of Change from Baseline in Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit for Subjects without Prior Exposure to CAB+RPV – LOCF (Maintenance Phase)	Adjust column header and footnote as appropriate.	W48

Health Outcomes Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
6.37	NA	NA	Intent-to-Treat Exposed	201585/primary_02/T7.33	Statistical Analysis of Change from Baseline in Acceptance/General Dimension Score (ACCEPT Questionnaire) by Visit for Subjects with Prior Exposure to CAB+RPV – LOCF (Maintenance Phase)	Adjust column header and footnote as appropriate.	W48
Preference							
6.38	NA	NA	Q4W ATLAS	Shell HO_T1	Proportion of Subjects with Response to Each Individual Question in Preference Questionnaire at Week 48 (Maintenance Phase) for Subjects from Q4W ATLAS to Q8W ATLAS-2M	Only display Q8W arm.	HL, W48
6.39	NA	NA	Intent-to-Treat Exposed	Shell HO_T1	Proportion of Subjects with Response to Each Individual Question in Preference Questionnaire by Prior Exposure to CAB+RPV (0 vs. >=1 Weeks) at Week 48 for Subjects in Q8W ATLAS-2M (Maintenance Phase)	Only display Q8W arm.	W48
6.40	NA	NA	Intent-to-Treat Exposed	Shell HO_T1	Proportion of Subjects with Response to Each Individual Question in Preference Questionnaire at Week 48 for Subjects in Q4W ATLAS-2M (Maintenance Phase)	Only display Q4W arm.	W48
Reasons for Switch/Continuation							
6.41	NA	NA	SOC	201585/primary_02/T7.40	Reasons for Switch at Baseline for Subjects from SOC	Remove columns 'Analysis Visit' and 'Total'. For percentages, use the format 'xx / xx (xx%)' where the denominator is the number of subjects with available valid data from the questionnaire.	W48

Health Outcomes Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
6.42	NA	NA	Q4W ATLAS	201585/primary_02/T7.40	Reasons for Continuation at Baseline for Subjects from Q4W ATLAS	Remove columns 'Analysis Visit' and 'Total'. For percentages, use the format 'xx / xx (xx%)' where the denominator is the number of subjects with available valid data from the questionnaire.	W48

15.14.5.11. Health Outcomes Figures

Health Outcomes Figures							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
6.1	NA	NA	Intent-to-Treat Exposed	201585/primary_02/F7.1	Line Plot of Adjusted Mean (95% CI) Change from Baseline in HIVTSQs Total Treatment Satisfaction Score over Time(ANCOVA) for Subjects without Prior Exposure to CAB+RPV - LOCF	Adjust footnotes as appropriate. Include Baseline as a timepoint in x axis.	W48
6.2	NA	NA	Intent-to-Treat Exposed	201585/primary_02/F7.1	Line Plot of Adjusted Mean (95% CI) Change from Baseline in HIVTSQs Total Treatment Satisfaction Score over Time(ANCOVA) for Subjects with Prior Exposure to CAB+RPV - LOCF	Adjust footnotes as appropriate. Include Baseline as a timepoint in x axis.	W48
6.3	NA	NA	Intent-to-Treat Exposed	201585/primary_02/F7.2	Line Plot of Difference (95% CI) in Adjusted Mean Change from Baseline in HIVTSQs Total Treatment Satisfaction Score over Time (ANCOVA) for Subjects without Prior Exposure to CAB+RPV - LOCF	Adjust footnotes as appropriate. Include Baseline as a timepoint in x axis.	W48
6.4	NA	NA	Intent-to-Treat Exposed	201585/primary_02/F7.2	Line Plot of Difference (95% CI) in Adjusted Mean Change from Baseline in HIVTSQs Total Treatment Satisfaction Score over Time (ANCOVA) for Subjects with Prior Exposure to CAB+RPV - LOCF	Adjust footnotes as appropriate. Include Baseline as a timepoint in x axis.	W48
6.5	NA	NA	Intent-to-Treat Exposed	201585/primary_02/F7.5	Line Plot of Adjusted Mean (95% CI) Change from Baseline in HAT-QoL (Life Satisfaction, HIV medication, and Disclosure Worries) by Visit (ANCOVA) for Subjects without Prior Exposure to CAB+RPV - LOCF	Adjust footnotes as appropriate. Include Baseline as a timepoint in x axis.	W48

Health Outcomes Figures							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
6.6	NA	NA	Intent-to-Treat Exposed	201585/primary_02/F7.5	Line Plot of Adjusted Mean (95% CI) Change from Baseline in HAT-QoL (Life Satisfaction, HIV medication, and Disclosure Worries) by Visit (ANCOVA) for Subjects with Prior Exposure to CAB+RPV - LOCF	Adjust footnotes as appropriate. Include Baseline as a timepoint in x axis.	W48
6.7	NA	NA	Intent-to-Treat Exposed	201585/primary_02/F7.6	Line Plot of Difference in Adjusted Mean (95% CI) Change from Baseline in HAT-QoL (Life Satisfaction, HIV Medication, and Disclosure Worries) by Visit (ANCOVA) for Subjects without Prior Exposure to CAB+RPV - LOCF	Adjust footnotes as appropriate. Include Baseline as a timepoint in x axis.	W48
6.8	NA	NA	Intent-to-Treat Exposed	201585/primary_02/F7.6	Line Plot of Difference in Adjusted Mean (95% CI) Change from Baseline in HAT-QoL (Life Satisfaction, HIV Medication, and Disclosure Worries) by Visit (ANCOVA) for Subjects with Prior Exposure to CAB+RPV - LOCF	Adjust footnotes as appropriate. Include Baseline as a timepoint in x axis.	W48

15.14.5.12. Virology Tables

Virology Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Genotype							
7.1	7.1	NA	Confirmed Virologic Failure	201585/primary_02/T8.1	Summary of the Prevalence of Known INI Resistance Mutations at time of CVF (Maintenance Phase) – Plasma Sample		W48, W96
7.2	7.2	NA	Confirmed Virologic Failure	201585/primary_02/T8.2	Summary of the Prevalence of Major Resistance Mutations of NRTI, NNRTI and PI Class at time of CVF (Maintenance Phase) - Plasma Sample		W48, W96
7.3	7.3	NA	Confirmed Virologic Failure	201585/primary_02/T8.4	Summary of Genotypic Susceptibility at time of CVF (Maintenance Phase) - Plasma Sample		W48, W96
Phenotype							
7.4	7.4	NA	Confirmed Virologic Failure	201585/primary_02/T8.3	Summary of Phenotype Susceptibility at time of CVF (Maintenance Phase) - Plasma Sample		W48, W96
7.5	7.5	NA	Confirmed Virologic Failure	201585/primary_02/T8.6	Summary of Phenotype: Number of Drugs to Which Subject is Phenotypic Resistant or Partial Sensitive or Sensitive at Time of CVF (Maintenance Phase) - Plasma Sample		W48, W96
7.6	7.6	NA	Confirmed Virologic Failure	201585/primary_02/T8.7	Summary of Fold Change to CAB and RPV at Time of CVF (Maintenance Phase) - Plasma Sample		W48, W96
7.7	7.7	NA	Confirmed Virologic Failure	201585/primary_02/T8.5	Summary of Net Assessment at time of CVF (Maintenance Phase) - Plasma Sample		W48, W96

Virology Tables							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Miscellaneousness							
7.8	7.8	NA	Confirmed Virologic Failure	201585/primary_02/T8.8	Summary of Viral load, Genotypic and Phenotypic data for Subjects Who Met Confirmed Virologic Failure Criteria during the Maintenance Phase	Remove columns for 'ARTs', 'FC for ARTs'. Adjust the footnotes as appropriate.	HL, W48, W96
NA	7.9	7.1	Confirmed Virologic Failure	201585/primary_02/T8.8	Summary of Viral load, Genotypic and Phenotypic data for Subjects Who Met Confirmed Virologic Failure Criteria during the Extension Phase	Remove columns for 'ARTs', 'FC for ARTs'. Adjust the footnotes as appropriate.	W96, EOS
7.9	7.10	7.2	Safety	201585/primary_02/T8.8	Summary of Viral load, Genotypic and Phenotypic data for Non-CVF Subjects with Genotypic and/or Phenotypic Data	Remove columns for 'ARTs', 'FC for ARTs'. Adjust the footnotes as appropriate.	W48, W96, EOS

15.14.5.13. ICH Listings

Note: Unless otherwise specified, both unique subject ID and latest subject ID for a subject will be included in the listings; display by prior exposure to CAB+RPV (0, 1-24, >24 weeks, refer to Section 15.6.2 for calculation details) for all listings except for study population listings.

ICH Listings							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Study Population							
1	1	1	Randomized	201585/primary_02/L1	Listing of Subjects Randomized but Not Treated		W48, W96, EOS
2	2	2	Randomized	201585/primary_02/L2	Listing of Randomized and Actual Strata and Treatment Assignment	Randomized and Actual Treatments will include oral lead-in information (e.g. Oral followed by Q4W). Change the footnote # for column 'Dev.' to be [2]. Add a footnote for actual strata: [1] Actual strata are derived using the prior exposure to CAB+RPV in Study 201585, collected from eCRF.	W48, W96, EOS
3	3	3	Screened	201585/primary_02/L3	Listing of Reasons for Screen Failure		W48, W96, EOS
4	4	4	Intent-to-Treat Exposed	ES2	Listing of Reasons for Study Withdrawal		HL, W48, W96, EOS
5	5	5	Intent-to-Treat Exposed	201585/primary_02/L5	Listing of Reasons for Study Drug Discontinuation		W48, W96, EOS

ICH Listings							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
6	6	6	Intent-to-Treat Exposed	201585/primary_02/L6	Listing of Important Protocol Deviations		W48, W96, EOS
7	7	7	Intent-to-Treat Exposed	201585/primary_02/L7	Listing of Protocol Deviations Leading to Exclusion from the Per-Protocol Population		HL, W48, W96, EOS
8	8	8	Intent-to-Treat Exposed	201585/primary_02/L8	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		W48, W96, EOS
9	9	9	Intent-to-Treat Exposed	201585/primary_02/L9	Listing of Demographic Characteristics		W48, W96, EOS
10	10	10	Intent-to-Treat Exposed	201585/primary_02/L10	Listing of Race		W48, W96, EOS
Efficacy							
11	11	11	Intent-to-Treat Exposed	201585/primary_02/L11	Listing of Study Outcome (50 c/mL Threshold) at Week 48 – Snapshot Analysis		HL, W48, W96, EOS
Safety: Exposure							
12	12	12	Safety	201585/primary_02/L12	Listing of Investigational Product Exposure Data		W48, W96, EOS

ICH Listings							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Safety: Adverse Events							
13	13	13	Safety	201585/primary_02/L13	Listing of Subject Numbers for Individual Adverse Events (Maintenance + Extension Phase)		W48, W96, EOS
14	14	14	Safety	201585/primary_02/L14	Listing of Reasons for Considering as a Serious Adverse Event (Maintenance + Extension Phase)		W48, W96, EOS
15	15	15	Safety	201585/primary_02/L15	Listing of Fatal Adverse Events (Maintenance + Extension Phase)	Add Study Period to the 5th Column from the left.	W48, W96, EOS
16	16	16	Safety	201585/primary_02/L16	Listing of Non-Fatal Serious Adverse Events (Maintenance + Extension Phase)	Add Study Period to the 5th Column from the left.	W48, W96, EOS
17	17	17	Safety	201585/primary_02/L17	Listing of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product (Maintenance + Extension Phase)	Add Study Period to the 5th Column from the left.	HL, W48, W96, EOS
18	18	18	Safety	201585/primary_02/L18	Listing of Changes in Intensity/Grades of Study Drug Injection Site Adverse Events (Maintenance + Extension Phase)		W48, W96, EOS
19	19	19	Safety	201585/primary_03/L30	Listing of All Adverse Events (Maintenance + Extension Phase)	Add Study Period to the 5th Column from the left.	W48, W96, EOS

ICH Listings							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Safety: Pregnancy							
20	20	20	Safety	201585/primary_02/L19	Listing of Subjects Who Became Pregnant during the Study (Maintenance + Extension Phase)		W48, W96, EOS

ICH Listings							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Safety: Hepatobiliary (Liver)							
21	21	21	Safety	201585/primary_02/L20	Listing of Medical Conditions for Subjects with Liver stopping Events		W48, W96, EOS
22	22	22	Safety	201585/primary_02/L21	Listing of Substance Use for Subjects with Liver Stopping Events		W48, W96, EOS
Safety: ECG							
23	23	23	Safety	201584/primary_01/L24	Listing of ECG Values for Subjects with a Value of Potential Clinical Importance	Remove Phase Treatment from the column header. Add change from baseline values for each of QTc assessment. Adjust the footnote as appropriate. A footnote may be added to clarify the classification of PCI values.	W48, W96, EOS
24	24	24	Safety	201584/primary_01/L23	Listing of ECG Findings		W48, W96, EOS
Safety: eC-SSRS							
25	25	25	Safety	201585/primary_02/L24	Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Section 1-Section 2)		W48, W96, EOS
26	26	26	Safety	201585/primary_02/L25	Listing of Possible Suicidality-Related Adverse Event Data: Possible Cause(s) (Section 3)		W48, W96, EOS
27	27	27	Safety	201585/primary_02/L26	Listing of Possible Suicidality-Related Adverse Event Data (Section 4)		W48, W96, EOS

ICH Listings							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
28	28	28	Safety	201585/primary_02/L27	Listing of Possible Suicidality-Related Adverse Event Data (Section 5-Section 8)		W48, W96, EOS
PK							
29	29	29	Pharmacokinetic	201584/primary_01/L30	Listing of Plasma CAB PK Concentration-Time Data	Remove 'Phase Treatment' from the column header.	W48, W96, EOS
30	30	30	Pharmacokinetic	201584/primary_01/L31	Listing of Plasma RPV PK Concentration-Time Data	Remove 'Phase Treatment' from the column header.	W48, W96, EOS

15.14.5.14. Non-ICH Listings

Note: Unless otherwise specified, both unique subject ID and latest subject ID for a subject will be included in the listings; display by prior exposure to CAB+RPV (0, 1-24, >24 weeks, refer to calculation details in Section 15.6.2) for all listings except for study population listings.

Non-ICH Listings							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Study Population							
31	31	31	Intent-to-Treat Exposed	201585/primary_02/L30	Listing of Reasons for Maintenance Phase Withdrawal		W48, W96, EOS
32	32	32	Oral Lead-in	201585/primary_02/L31	Listing of Reasons for Oral Lead-in Period Withdrawal		W48, W96, EOS
NA	33	33	Intent-to-Treat Exposed	201585/primary_02/L32	Listing of Reasons for Extension Phase Withdrawal		W96, EOS
33	34	34	Long-term Follow-up	201585/primary_02/L33	Listing of Reasons for Long-term Follow-up Phase Withdrawal		W48, W96, EOS
34	35	35	Screened	Shell POP_L2	Listing of Subjects Who were Rescreened		W48, W96, EOS
35	36	36	Intent-to-Treat Exposed	Shell POP_L1	Listing of Prior ART Medications	Remove the column 'Phase during Which Concomitant'	W48, W96, EOS
36	37	37	Intent-to-Treat Exposed	Shell POP_L1	Listing of Concomitant ART Medications	In case the same medication is concomitant during both maintenance and extension phases, list each of them in two separate rows.	W48, W96, EOS

Non-ICH Listings							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
37	38	38	Intent-to-Treat Exposed	Shell POP_L1	Listing of ART Medications Received during Long-term Follow-up Phase	Remove the column 'Phase during Which Concomitant'	W48, W96, EOS
38	39	39	Intent-to-Treat Exposed	201585/primary_02/L39	Listing of Investigational Product Accountability - Oral Regimens		W48, W96, EOS
39	40	40	Intent-to-Treat Exposed	201584/primary_01/L43	Listing of Medical History of Seizure		W48, W96, EOS
Efficacy							
40	41	41	Confirmed Virologic Failure	201585/primary_02/L40	Listing of All Plasma HIV-1 RNA data for subjects with Confirmed Virologic Failure	In column headers, replace 'Period' with 'Phase', replace 'Sample Day' with 'Study Day'.	W48, W96, EOS
41	42	42	Intent-to-Treat Exposed	201585/primary_02/L41	Listing of All Plasma HIV-1 RNA data for subjects with viral load >=50 c/mL during the Maintenance Phase	In column headers, replace 'Period' with 'Phase', replace 'Sample Day' with 'Study Day'.	HL, W48, W96, EOS
42	NA	NA	Oral Lead-in	201585/primary_02/L41	Listing of All Plasma HIV-1 RNA data for subjects with viral load >=50 c/mL during the Maintenance Oral Lead-in Period	In column headers, replace 'Period' with 'Phase', replace 'Sample Day' with 'Study Day'.	W48
43	43	43	Intent-to-Treat Exposed	201585/primary_02/L43	Listing of HIV-1 Associated Conditions (Maintenance + Extension Phase)		W48, W96, EOS
Safety (list data during Maintenance and Extension Phases, unless otherwise specified)							
44	44	44	Safety	ABC_HSR_EXPO2	Listing of Abacavir Hypersensitivity Reaction Record - Exposure to Abacavir		W48, W96, EOS

Non-ICH Listings							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
45	45	45	Safety	ABC_HSR_DRUG2	Listing of Abacavir Hypersensitivity Reaction Record - Subject History of Drug Allergies		W48, W96, EOS
46	46	46	Safety	ABC_HSR_COND2	Listing of Abacavir Hypersensitivity Reaction Record - Subject and Family Conditions		W48, W96, EOS
47	47	47	Safety	ABC_HSR_RASH2	Listing of Abacavir Hypersensitivity Reaction Record - Skin Rash Details		W48, W96, EOS
48	48	48	Safety	ABC_HSR_SYMP4	Listing of Abacavir Hypersensitivity Reaction Record - Symptoms		W48, W96, EOS
49	49	49	Safety	VS4	Listing of Abacavir Hypersensitivity Reaction Record - Vital Signs		W48, W96, EOS
50	50	50	Safety	ABC_HSR_SYMP6	Listing of Abacavir Hypersensitivity Reaction Record - Individual Symptoms and Diagnostic Category Assignments (Excluding Other Symptoms)		W48, W96, EOS
51	51	51	Safety	ABC_HSR_SYMP7	Listing of Abacavir Hypersensitivity Reaction Record - Individual Symptoms and Diagnostic Category Assignments (Other Symptoms)		W48, W96, EOS
52	52	52	Safety	201585/primary_02/L52	Listing of Liver monitoring/stopping Event Reporting		W48, W96, EOS
53	53	53	Safety	201585/primary_02/L53	Listing of Liver Event Information for RUCAM Score		W48, W96, EOS
54	54	54	Safety	201585/primary_02/L54	Listing of Liver Biopsy Details		W48, W96, EOS
55	55	55	Safety	201585/primary_02/L55	Listing of Liver Imaging Details		W48, W96, EOS

Non-ICH Listings							
No. in W48	**No. in W96**	**No. in EOS**	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
56	56	56	Safety	201585/primary_02/L59	Listing of Subjects Meeting Hepatobiliary Lab Criteria (Maintenance + Extension Phase)		W48, W96, EOS
57	57	57	Safety	201585/primary_02/L57	Listing of Potential QTc Interval Prolonging Events of Interest	Add Study Period to the 5th Column from the left.	W48, W96, EOS
58	58	58	Safety	201585/primary_02/L58	Listing of ECG values for Subjects with Potential QTc Interval Prolonging Events of Interest		W48, W96, EOS
59	59	59	Safety	201584/primary_01/L64	Listing of ALT, AST, Bilirubin (including Total and Direct Bilirubin), INR, and ALP for Subjects Meeting Hepatobiliary Lab Abnormality Criteria	Remove 'Only Q4W IM Subjects are presented in this listing.' from the footnote.	HL, W48, W96, EOS
60	60	60	Safety	201585/primary_02/L63	Listing of Investigational Product Exposure Data for Subject Receiving Oral Bridging		W48, W96, EOS
61	61	61	Safety	201584/primary_01/L66	Listing of Dosing Errors and IP Device Malfunctions		W48, W96, EOS
Virology							
62	62	62	Confirmed Virologic Failure	201585/primary_02/64	Listing of Replication Capacity in IN and PR/RT Region	Remove 'of Maintenance Phase' from the column header 'Study Day of Maintenance Phase'.	W48, W96, EOS

15.15. Appendix 15: Example Mock Shells for Data Displays

Available upon request