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

Title	:	**A Phase 1, Open-Label Study to Evaluate the Pharmacokinetics and Tolerability of Cabotegravir and Rilpivirine Long-Acting Injections Following Intramuscular Administration in the *Vastus Lateralis* Muscle of Healthy Adult Participants**
Compound Number	:	GSK1265744
Effective Date	:	07-MAY-2021

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 208832
- This RAP is intended to describe the safety, pharmacokinetics, and tolerability analyses required for the study
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.

RAP Author(s):

Author	Date
Lead	07-MAY-2021
PPD Statistician (HIV, GSK Clinical Statistics)	
Co-Authors	07-MAY-2021
PPD Principal Programmer (HIV, GSK Clinical Programming)	

RAP Team Review Confirmations: (Method: E-mail)

Reviewer	Date
PPD Clinical Development Manager (R&D GCSD, GSK)	07-MAY-2021
PPD Principal Clinical Data Manager (GCDO, GSK Clinical Data Management)	06-MAY-2021
PPD Manager, Clinical Pharmacology (GSK CPMS)	06-MAY-2021
PPD PPD, Research & Development (ViiV Healthcare)	06-MAY-2021

Clinical Statistics & Clinical Programming Line Approvals: (Method: Pharma TMF eSignature)

Approver	Date
PPD Statistics Leader (HIV, GSK Clinical Statistics)	05-MAY-2021
PPD Programming Director (HIV, GSK Clinical Programming)	07-MAY-2021

TABLE OF CONTENTS

PAGE

1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Pharmacology Study Report for Protocol 208832.
Protocol	This RAP is based on the original protocol (Dated 02-MAR-2020) of study GSK1265744/208832 (GSK Document No.: 2018N357118_00) and its protocol amendment 1 (Dated 13-AUG-2020; GSK Document No.: 2018N357118_01)
Primary Objective	To describe the PK profiles of CAB and RPV following a single intramuscular injection each of CAB LA + RPV LA administered to the lateral thigh muscle in adult healthy participants
Primary Endpoint	• Maximum observed concentration (C_{max}) and time of maximum observed concentration (t_{max}) in plasma • Area under the concentration – time curve from time zero to last quantifiable time point (AUC_{0-t}) through the follow-up phase • Area under the concentration – time curve from time zero to infinity ($AUC_{0-\infty}$) • Apparent terminal phase half-life (t½) and absorption rate constant (K_A LA)
Study Design	This is a Phase 1, open label study conducted in healthy participants to assess the PK of CAB and RPV in plasma following a single 600 mg (1 x 3 mL) and a 900 mg (1 x 3 mL) injection each, respectively, administered IM to separate *vastus lateralis* muscles on each leg. The study will consist of a 30-day screening phase, a 28-day oral lead-in (OLI) phase at a CAB dose of 30 mg and RPV dose of 25 mg once a day with a meal, followed by a 10-14 day washout phase. Single doses of CAB and RPV will then be injected, administered IM: 600 mg (1 x 3 mL) CAB on left and a 900 mg (1 x 3 mL) RPV injection on right *vastus lateralis* muscles. Sparse PK sampling for up to 29 days in OLI and serial PK sampling for up to 4 weeks after the injection, per SoA. Participants will return for safety assessments and additional PK sampling at Week 8, 12, 24, 36, and 52 post last injection during the follow-up phase.
Planned Analyses	All the derived PK parameters will be listed and summarized by treatment and study phase. For each of these PK parameters the following descriptive summary statistics will be calculated: n, arithmetic mean with associated 95% CI, standard deviation, median, minimum, and maximum. The mean & geometric mean with associated 95% CIs, standard deviations, and geometric coefficient of variation (CV_b(%)) will be calculated for all parameters except t_{tmax}.
Analysis Populations	Enrolled Population, Safety Population, Pharmacokinetic Concentration Population and Pharmacokinetic Parameter Population
Hypothesis	No formal hypothesis will be tested in this study
Primary Analyses	Primary endpoints include CAB and RPV PK parameters C_{max}, AUC_{0-t}, $AUC_{0-\infty}$, $t_{1/2,}$ and K_A LA as calculated from injection phase concentration-time data. Descriptive statistics and graphics will be created to describe the primary PK endpoints of interest.

1.1. Revision Chronology

Revision Chronology:		
ID: 35421_2099331	31-AUG-2020	Critical Components

2. SUMMARY OF KEY PROTOCOL INFORMATION

Cabotegravir (CAB) is an integrase inhibitor being developed in combination with rilpivirine (RPV, TMC278), a non-nucleoside reverse transcriptase inhibitor, for the treatment of HIV. CAB is currently in Phase 3 development as monotherapy for the prevention of sexually-acquired HIV-1 infection. CAB and RPV are separately formulated as oral tablets for once daily administration and as long-acting (LA) aqueous suspensions for parenteral administration monthly or every 2-months. RPV 25mg oral tablets is approved as EDURANT in multiple countries, including the USA, Europe and Canada, for use in antiretroviral (ARV) treatment-naïve patients.

A two-drug long-acting, monthly antiretroviral regimen of CAB + RPV has demonstrated good efficacy, tolerability, and long-term safety in HIV-infected adults following oral and monthly and every 2-month IM dosing in the gluteus muscle for durations exceeding 3 years in Phase 2 and Phase 3 studies [LATTE; LATTE-2; ATLAS, 2019; FLAIR, 2019, ATLAS-2M]. Review and approval of the CAB + RPV regimen for treatment of HIV infection is ongoing.

Separate early Phase 1 studies of CAB LA and RPV LA evaluated PK and tolerability of single and repeat-dose injections in other anatomic locations including abdomen (subcutaneous) and IM administration in the ventrogluteal muscle (CAB), gluteus maximus muscle (RPV), and deltoid muscle (RPV) in healthy volunteers [HIV Therapy 2013; International AIDS Society 2013; RPV LA NATAP report]. Gluteal injections of CAB LA + RPV LA were progressed in late-stage studies given better participant tolerability to injections at this injection site with the anticipated injection dosing volume required to achieve desired exposures.

There remains considerable interest in exploring alternative injection sites either as an alternative rotational (e.g. gluteal injection fatigue) or chronic injection site (e.g. gluteal implants contraindicating injection or young pediatric populations without sufficient gluteal mass for injection). The *vastus lateralis* muscle in the thigh has been used as an injection location for other drugs (e.g. epinephrine, etc.) and is a common injection site in young children (e.g. vaccines). Moreover, self- or partner-injection of CAB LA + RPV LA in the thigh muscle may be explored in future studies pending favorable pharmacokinetics, safety, and tolerability of CAB LA + RPV LA thigh injections.

The objective of this study is to evaluate the pharmacokinetics, tolerability, and safety of CAB LA + RPV LA administered concomitantly as two separate IM injections in the *vastus lateralis* muscle of adult healthy participants. Data from this study will be used to inform the feasibility of administering CAB LA + RPV LA in the *vastus lateralis* muscle in HIV-infected children <12 years of age and adult populations.

2.1. Changes to the Protocol Defined Statistical Analysis Plan

In consideration of the recent, global Covid-19 pandemic, and in accordance with recent GSK clinical guidance, sensitivity analyses summarizing disposition and select safety results will be displayed alongside primary results. This stands as an addition to the originally planned statistical analysis specified in the protocol dated 02-MAR-2020 and

protocol amendment 1 dated 13-AUG-2020. A second addition will be the calculation of PK parameters in the OLI phase alongside the PK parameters of the Injection phase as noted in the primary objective. Thirdly, the protocol calls for the short version CCI questionnaire to be implemented while this RAP plans for the full version, administered separately for each thigh, in order to collect clinically meaningful information on the future use of thigh injections in the pediatric population. Finally, listings are specified to be inclusive of all screened subjects.

Changes from the originally planned statistical analysis specified in the protocol and its amendment 1 are outlined in Table 1.

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	Reporting & Analysis Plan	Rationale
• Study objectives and endpoints listed without consideration of the Covid-19 pandemic	• Disposition and select safety results will be repeated with consideration to subjects' relation to Covid-19.	• The Covid-19 pandemic has spurred the need to assess whether the impact creates substantial impact on study results.
• PK parameters only calculated for Injection phase	• Applicable PK parameters will also be calculated in the OLI phase as data permits	• OLI PK parameters are of interest in addition to Injection parameters
• Short version of CCI questionnaire recorded	• Full version of the CCI questionnaire recorded separately for each injection	• Information found in the full version is considered clinically meaningful to plan for further thigh injections in children.
• PK Listings are subset by population relevant to the data	• All listing data will be shown for all screened subjects	• To more feasibly serve as a reference for subjects not meeting population requirements

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

Table 2 Study Objectives and Endpoints

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To describe the PK profiles of CAB and RPV following a single intramuscular injection each of CAB LA + RPV LA administered to the lateral thigh muscle in adult healthy participants.	• Maximum observed concentration (C_{max}) and time of maximum observed concentration (t_{max}) in plasma • Area under the concentration – time curve from time zero to last quantifiable time point (AUC_{0-t}) through the follow-up phase • Area under the concentration – time curve from time zero to infinity ($AUC_{0-\infty}$) • Apparent terminal phase half-life ($t_{½}$) and absorption rate constant (K_A LA)

Safety Objectives	Safety Endpoints
• To assess safety and tolerability of CAB and RPV following repeated oral dose and single intramuscular injection in the lateral thigh of healthy participants	• Safety and tolerability parameters including adverse events (AEs), clinical laboratory tests, electrocardiogram (ECG), and vital sign assessments
Secondary Objectives	**Secondary Endpoints**
• To assess liver safety and tolerability of CAB and RPV following repeated oral dose and single intramuscular injection in the lateral thigh of adult healthy participants	• Tolerability parameters (liver related adverse events) and liver chemistry abnormalities
Exploratory Objectives	**Exploratory Endpoints**
CCI [redacted]	

2.3. Study Design

This is a phase 1, open label study in healthy participants to assess the PK of CAB and RPV in plasma following a single 600 mg (1 x 3 mL) and a 900 mg (1 x 3 mL) injection each; respectively, administered IM to separate *vastus lateralis* muscles on each leg.

The study will consist of

- 30-day screening period
- 28-day oral lead-in (OLI) phase at a CAB dose of 30 mg and RPV dose of 25 mg once a day with a meal
- 10 – 14 days washout period
- CAB and RPV injection, administered IM: 600 mg (1 x 3 mL) CAB on left and a 900 mg (1 x 3 mL) RPV injection on right *vastus lateralis* muscle
- Sparse PK sampling for up to 29 days in OLI and serial PK sampling for up to 4 weeks after the injection, per SoA. Participants will return for safety assessments and additional PK sampling at Week 8, 12, 24, 36, and 52 post last injection during the follow-up phase.

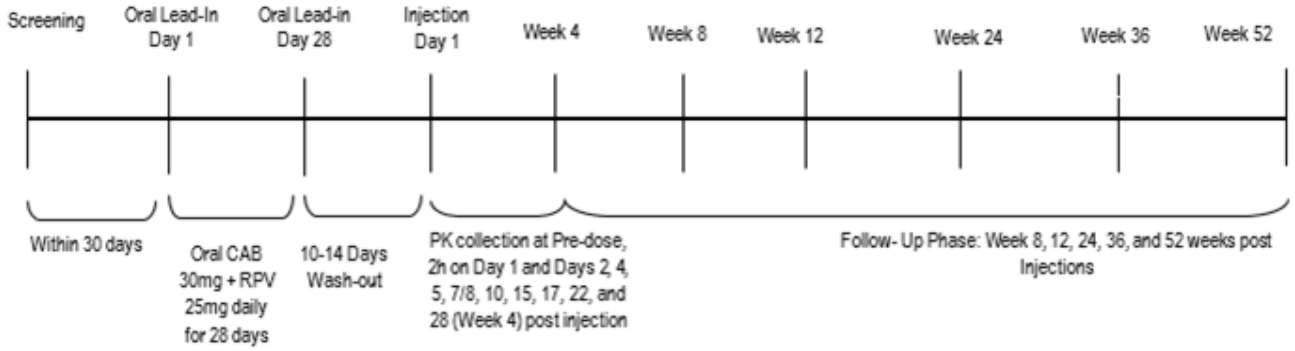
Approximately 15 adult healthy participants will be dosed with injectable study interventions. If participants prematurely discontinue the study, for any other reason,

other than an AE, additional replacement participants may be enrolled at the discretion of the Sponsor in consultation with the investigator. The study design is defined in Table 3.

Table 3 Study Design

Screening	Oral Lead-in	Washout	CAB Injection and Compartmental PK Sampling	Safety/ Blood Plasma Sampling
Within 30 days of Oral Lead-in	Oral CAB 30 mg tablet + Oral RPV 25 mg tablet once daily x 28 days	No drug administered 10 - 14 days	Single 600 mg CAB LA IM dose into lateral thigh + single 900 mg RPV LA IM dose into opposite lateral thigh Serial blood plasma sampling up to 4 weeks post-injection	Follow-up safety assessments and blood plasma PK sampling will occur at 8, 12, 24, 36, and 52 Weeks post-dose

Figure 1 Study Schematic



Injection Day 1: CAB LA 600mg IM (3mL) + RPV LA 900mg IM (3mL) Lateral thigh

2.4. Statistical Hypotheses

2.4.1. Hypotheses

The primary objective of this study is to describe the PK profiles of CAB and RPV following a single intramuscular injection each of CAB LA + RPV LA administered to the lateral thigh muscle. No formal statistical hypotheses are to be tested. Where appropriate, an estimation approach will be taken, and point estimates and confidence intervals will be constructed. There will be no formal comparison.

3. PLANNED ANALYSES

3.1. Interim Analyses

There will be no formal interim analysis. All preliminary safety, tolerability and available pharmacokinetic data may be reviewed internally at any time point. Depending on feasibility, evaluation of PK data may be performed at time points such as Week 4 and Week 12 post injection for preliminary PK analysis.

3.2. Final Analyses

Final analysis will be performed after all subjects have completed the study and final database freeze (DBF) has been declared by Data Management. Data will be listed and summarized according to GSK reporting standards, where applicable.

Statistical data analyses will be performed by, or under the direct auspices of, Clinical Statistics and Programming, GlaxoSmithKline utilizing SAS version 9.4 or higher. PK analysis of the plasma CAB and RPV concentration-time data will be conducted using non-compartmental methods with WinNonlin (Version 6.3 or higher).

All the derived PK parameters will be listed and summarized by treatment and study phase. For each of these PK parameters the following descriptive summary statistics will be calculated: n, arithmetic mean with associated 95% CI, standard deviation, median, minimum, and maximum. The mean & geometric mean with associated 95% CIs, standard deviations, and geometric coefficient of variation (CV_b(%)) will also be calculated for all parameters except t_{max}.

Safety and health outcome data will be presented in tabular and/or graphical format and summarized descriptively according to GSK's Integrated Data Standards Library (IDSL) standards.

4. ANALYSIS POPULATIONS

As a convention, listing data will be displayed for all screened subjects.

Table 4 Study Populations

Population	Definition / Criteria	Analyses Evaluated
Enrolled	• All participants who sign the ICF. • Note screening failures (who never passed screening even if rescreened) and participants screened but never enrolled into the study are excluded from the Enrolled population as they did not enter the study.	• Study Population
Safety	• All participants who take at least 1 dose of study drug.	• Study Population • Safety
Pharmacokinetic Concentration (PC)	• All participants who undergo plasma PK sampling and have evaluable PK assay results from either oral or injection dosing	• Concentration summaries • Individual plotting of concentration-time data
Pharmacokinetic Parameter (PP)	• All participants who undergo plasma PK sampling and have evaluable PK parameters estimated. • Note: PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded.	• PK parameter summaries • Mean/median plots and summary tables

Refer to Appendix 9: 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, excluded medications, conduct of the trial, participant management, or participant assessment) will be summarized with frequencies and proportions by study phase and overall.

Protocol deviations will be tracked by the study team throughout the conduct of the study.

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

All protocol deviations will be listed. A separate listing of all inclusion/exclusion criteria deviations will also be provided. This listing will be based on data as recorded on the inclusion/exclusion page of the electronic case report form (eCRF).

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Treatment and Other Sub-Group Descriptions for Data Displays

Data display treatment descriptors with actual treatment dose will be defined as displayed in Table 5. Safety events in the washout phase will be counted with events in the Oral lead-in phase. Safety events in the Follow-up phase will be counted separately from the Injection phase.

Table 5 Study Treatment

	Treatment Group Descriptions				
Phase	**Analysis**	**Data Set**		**Final Data Display (i.e. HARP / other)**	
		Code	**Treatment Description**	**Treatment Description-Footnote**	**Column Header**
Oral Lead-in	PK	A	Oral CAB 30mg tablet once daily x 4 weeks lead-in	Oral CAB 30mg=Cabotegravir 30mg PO 4 weeks lead-in	Oral CAB 30mg
		B	Oral RPV 25mg tablet once daily x 4 weeks lead-in	Oral RPV 25mg= Rilpivirine 25mg PO 4 weeks lead-in.	Oral RPV 25mg
	Safety	AB	Oral CAB 30mg + RPV 25mg tablets once daily x 4 weeks lead-in	Oral CAB 30mg + Oral RPV 25mg =Cabotegravir 30mg + Rilpivirine 25mg PO 4 weeks lead-in	Oral CAB 30mg + Oral RPV 25mg
Injection, Follow-up	PK, Safety (ISRs), HO	C	Single 600mg CAB LA IM dose	IM CAB 600mg=Cabotegravir IM 600mg single dose.	IM CAB 600mg – Injection Phase; IM CAB 600mg – Follow-up Phase
		D	Single 900mg RPV LA IM dose	IM RPV 900mg=Rilpivirine IM 900mg single dose.	IM RPV 900mg – Injection Phase; IM RPV 900mg – Follow-up Phase
	Safety	CD	Single 600mg CAB + single 900mg RPV LA IM dose	IM CAB 600mg + IM RPV 900mg = Cabotegravir IM 600mg + Rilpivirine IM 900mg single dose.	IM CAB 600mg + IM RPV 900mg – Injection Phase; IM CAB 600mg + IM RPV 900mg – Follow-up Phase

5.2. Baseline Definitions

For safety parameters the baseline or pre-dose value will be the latest assessment prior to the time of study drug administration in each phase with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and considered for use as baseline. If there are multiple assessments collected on the same scheduled time, the average of these assessments will be used. Table 6 indicates the baseline day to be used in the analysis.

Table 6 Baseline Parameter Specifications

Phase	Parameter	Study Assessments Considered as Baseline	Baseline Used in Data Display
Oral Lead-in Phase	Laboratory results, Vital Sign results, ECG results[1]	OLI Baseline = last non-missing pre-dose assessment collected <= Date of first OLI dose	OLI Day 1
Injection Phase	Laboratory results, Vital Sign results (pre-dose), ECG results[1] (pre-dose), CCI scores	Injection Phase Baseline = assessment collected on the date of CAB + RPV injection	Injection Day 1
Follow-up Phase	Laboratory results, Vital Sign results (pre-dose), ECG results[1] (pre-dose)	Follow-up Phase Baseline = assessment collected on the date of CAB + RPV injection	Injection Day 1

1. Average of the triplicate assessments for quantitative assessments will be used as the baseline.

If time is not collected, Day 1 assessments are assumed to be taken prior to first dose of the respective phase. Unless otherwise stated, if baseline data is missing no derivation will be performed and baseline will be set to missing.

5.3. Other Considerations for Data Analyses and Data Handling Conventions

5.3.1. Other Considerations

Other considerations for data analyses, including information regarding premature withdrawal, unscheduled assessments, derived and transformed data, and data handling conventions are outlined in the appendices:

Section	Component
11.1	Appendix 1: Schedule of Activities
11.2	Appendix 2: Assessment Windows
11.3	Appendix 3: Study Phases and Treatment Emergent Adverse Events
11.4	Appendix 4: Data Display Standards and Handling Conventions
11.5	Appendix 5: Derived and Transformed Data
11.6	Appendix 6: Reporting Standards for Missing Data

Section	Component
11.7	Appendix 7: Values of Potential Clinical Importance
11.8	Appendix 8: Abbreviations & Trademarks
11.9	Appendix 9: List of Data Displays
11.10	Appendix 10: AESI Identification

6. STUDY POPULATION

The study population analyses will be based on both the Enrolled and Safety populations, unless otherwise specified.

Study population analyses include analyses of study populations, subjects' disposition, important protocol deviations, demographic and baseline characteristics, and prior and concomitant medications. Outputs will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 9: List of Data Displays.

6.1. Subject Disposition

A summary table will be generated to provide the count of subjects included in each analysis population for the study (see Section 4 for definition of analysis populations).

The End of Study Record will be summarized by study phase and overall. Counts for the all discontinuation categories will be repeated considering subjects who discontinued to a Covid-19 related incident.

A disposition listing will include whether subjects prematurely withdrew from the study, the reason for premature discontinuation along with the start and end date of investigational product (IP) dosing and the date of completion or premature discontinuation from the study. An additional listing showing subjects who discontinued to Covid-19 considerations will be included.

6.2. Demographic and Baseline Characteristics

Demographic data include date of birth, sex, race, and ethnicity. Demographic data and baseline characteristics (i.e. height, weight, and BMI) will be summarized for the Safety Population. Race will be further summarized separately from the other demographic characteristics. All demographic data will be listed by subject.

6.3. Medical History and Concomitant Medications

Medical history events will be summarized and listed. Concurrent medication verbatim text will be coded and classified by the Anatomical Therapeutic Chemical Classification level 1 (ATC Level 1) code and the preferred term using the GSK coding system, GSK DRUG. Concomitant medications will then be summarized by ATC classification, study phase, and overall. Coding of concurrent medications will be the responsibility of the GSK coding group.

7. SAFETY ANALYSES

Safety data will be summarised and listed by, or under the direct auspices of, Clinical Statistics, GlaxoSmithKline. The safety summaries will be based on the Safety population, unless otherwise specified and shown for the Oral Lead-in, Injection, and Follow-up phases where applicable.

Safety endpoints include:

- Safety and tolerability parameters including adverse events, clinical laboratory tests, ECG, and vital sign assessments
- Tolerability parameters (liver related adverse events) and liver chemistry abnormalities

For continuous safety parameters, the Injection phase Baseline will also serve as Follow-up phase Baseline. No formal statistical analysis of the safety data will be conducted. The precise format and content of Safety tables and listings are shown in Appendix 9 of the RAP.

7.1. Extent of Exposure and Treatment Compliance

Overall CAB & RPV exposure will be presented with descriptive statistics (i.e. n, mean, SD, median, minimum, and maximum) by study phase and treatment. Treatment will be determined by the laterality of the injection. CAB will be administered on a subject's ***left*** thigh while RPV will be administered on a subject's ***right*** thigh. Parameters displayed will include number of days of oral exposure, oral compliance percentage, and injection status. Details on oral compliance percentage calculation are included in Appendix 5.

A by-subject listing of data on subject exposure will be generated including dose date and time, unit, formulation, route, frequency and location.

7.2. Adverse Events

Adverse event verbatim text will be coded and classified by system organ class (body system) and preferred term using a standardized GSK coding system: Medical Dictionary for Regulatory Activities (MedDRA, v23.0 or higher). AE data will be summarized with frequencies and percent by study phase and overall. The relationship of AE system organ class, preferred term, and verbatim text will be listed. Treatment emergent AEs, drug-related AEs, serious adverse events (SAEs) including fatal AEs, and AEs leading to drug withdrawal or study discontinuation will be summarized by study phase and overall. AEs and drug-related AEs will also be summarized by maximum toxicity grade (based on Division of AIDS (DAIDS) categories). All AEs will be listed by subject and AE start date.

Adverse events related to Covid-19 will also be summarized by SOC, PT, and maximum toxicity. Subjects with Covid-19 tests performed as well as Covid-19 diagnoses will also be summarized. Summaries of serious Covid-19 AEs and Covid-19 AEs leading to study discontinuation or drug withdrawal will also be presented in accordance with Covid-19 safety assessment guidance. Covid-19 AEs will also be presented by sex and pandemic course (during and post-) if applicable.

7.3. Injection Site Reaction Adverse Events

Injection site reaction adverse event data will also be summarized by treatment and overall. Tables will include subject and event-level summaries. ISR treatment will be determined by the laterality of the assessment (left vs. right). All ISR AEs will be shown in a separate listing from overall adverse events.

7.4. Adverse Events of Special Interest (AESIs)

AESIs will be summarized for Hepatotoxicity and Seizures. QT Prolongation events will be listed. A comprehensive list of MedDRA terms based on clinical review will be used to identify each type of event for Adverse Events of Special Interest (AESI). [Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting and/or emerging data from on-going studies may highlight additional adverse events of special interest, therefore the list of terms to be used for each event of interest and the specific events of interest will be based on the safety review team (SRT) agreements in place at the time of reporting.] The details of the current planned grouping, including Standardized MedDRA Query (SMQ) values (as applicable), and planned displays are provided in Appendix 10: AESI Identification and Appendix 9: List of Data Displays.

7.5. Pregnancies (as applicable)

If any female subjects become pregnant during the study, a listing of such subjects will be provided.

7.6. Clinical Laboratory Evaluations

Worst grade post-baseline for hematology, clinical chemistry, and urinalysis data will be summarized by study phase. Summaries of change from baseline in hematology and clinical chemistry by study phase and visit will be created. If any laboratory test results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing. Standardized units will be used for clinical laboratory summary tables and listings.

Hematology, clinical chemistry, drug, infectious disease, coagulation and urinalysis data will be listed by subject, study phase, visit, and collection date.

7.7. Other Safety Analyses

Vital sign data (temperature, systolic and diastolic blood pressure, and pulse rate) will be summarized by study phase, visit, and planned time. Absolute values and change from baseline values will be shown. Injection phase Baseline will also serve as Follow-up phase Baseline. Vitals signs will be listed by subject, study phase, visit, planned time, and actual date and time.

Electrocardiogram (ECG) data including values and findings will be summarized by study phase, visit, and timepoint. Absolute values and change from baseline will be shown for PR, QRS, QT, QTcB, and QTcF results. Baseline will be calculated as the mean of triplicate readings recorded prior to first dose in each study phase.

All ECG data including clinical interpretation will be listed by subject, study phase, visit and record date. Clinically significant ECG abnormalities will be flagged and listed separately, and corresponding values will be provided.

Liver related adverse events and chemistry abnormalities will be summarized separately by study phase. See Appendix 10 for a list of Hepatotoxicity AEs and Appendix 7 for Chemistry values of Potential Clinical Importance.

8. PHARMACOKINETIC ANALYSES

The reconciliation of the PK Case Report Form (CRF) and SMS2000 data will be performed by, or under the direct auspices of, Clinical Pharmacology Sciences and Study Operations (CPSSO), GlaxoSmithKline.

The merge of PK concentration data and CRF data will be performed by, or under the direct auspices of, Clinical Statistics (Programmer), GlaxoSmithKline.

Derivation of pharmacokinetic parameters will be performed by, or under the direct auspices of, Clinical Pharmacology Modelling and Simulation (CPMS), GlaxoSmithKline.

Statistical analysis of pharmacokinetic parameters will be performed by, or under the direct auspices of, Clinical Statistics (Statistician), GlaxoSmithKline.

Concentration and PK parameter data will be reported for specified Pharmacokinetic populations in the OLI and Injection phases.

8.1. Drug Concentration Measures

Plasma CAB and RPV concentration values will be summarized with descriptive statistics by study phase, treatment, visit, and planned timepoint for the PK Concentration Population (PC). These concentration values will be determined directly from concentration-time data from each analyte. Descriptive statistics including the n, mean with associated 95% CI, standard deviation, median, minimum, maximum, geometric mean with associated 95% CI, standard deviation of logarithmically transformed data, $5^{th}/95^{th}$ percentiles and the geometric coefficient of variation ($CV_b(\%)$)).

Individual concentration-time profiles and median/mean profiles from each analyte in each study phase will be plotted for the PK Concentration (PC) Population. Each of the figures will contain one plot on the untransformed scale (i.e. a linear plot) and one plot on the log transformed scale (i.e. semi-log plot). Actual assessment times will be used in the individual concentration-time plots. Nominal times will be used for the purposes of summarization and in mean and median plots. See Appendix 4: Data Display Standards & Handling Conventions. for details on pharmacokinetic figure and table displays.

8.2. Deriving and Summarizing Pharmacokinetic Parameters

Pharmacokinetic parameters will be derived by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin 6.3 or higher (Pharsight, Inc., Cary, NC). All calculations of non-compartmental PK parameters will be based on actual sampling times. Pharmacokinetic parameters listed will be determined from the plasma concentration-time data, as data permits. The following PK parameters will be derived and displayed for the PP Population as data permits:

Table 7 Derived PK Parameters

Parameter	Parameter Description	OLI Phase	Injection Phase
C_{max}	Maximum observed concentration	Day 1	Overall
t_{max}	Time of occurrence of C_{max}	Day 1	Overall
$AUC_{0-\infty}$	Area under the concentration time curve from time zero to infinity	Day 1-2	Overall
AUC_{0-t}	Area under the concentration time curve from time zero to last quantifiable time point	Day 1-2	Overall
$t_{1/2}$	Terminal phase half-life	Day 1-2	Overall
K_A LA	Absorption rate constant, Long-acting	NA	Overall
λz	Terminal phase rate constant	Day 1-2	NA
C24	Concentration at OLI Phase 24-hour timepoint	Day 2	NA
$C\tau$	Trough concentrations ($C\tau$) at OLI Phase Day 29	Day 29	NA

NOTES: NA: Not Applicable

- Additional parameters may be included as required.

Primary Pharmacokinetic endpoints include the following PK parameters from Injection Phase:

- Maximum observed concentration (Cmax) and time of maximum observed concentration (t_{max}) in plasma
- Area under the concentration – time curve from time zero to last quantifiable time point (AUC_{0-t}) through the follow-up phase
- Area under the concentration – time curve from time zero to infinity ($AUC_{0-\infty}$)
- Apparent terminal phase half-life ($t½$) and absorption rate constant (K_ALA))

PK parameters such as C_{max} and AUC should be reported in µg/mL and µg*h/mL for CAB and in ng/mL and ng*h/mL for RPV. Other PK parameters such as t_{max} and $t_{1/2}$ should be reported in hours and K_ALA and λz parameters in /h for both CAB and RPV.

8.3. Statistical Analyses

All the derived pharmacokinetic parameters will be summarized and listed for the PP population by study phase and treatment. For each of these PK parameters, with the exception of t_{max}, the following descriptive summary statistics will be calculated for each treatment: n, arithmetic mean with associated 95% CI, standard deviation, median, minimum, maximum, geometric mean with associated 95% CI, standard deviation of logarithmically transformed data, and the geometric coefficient of variation (CV_b(%)). For t_{max}, the n, median, minimum, and maximum summary statistics will be provided.

Data display specifications for derived PK parameter summaries and listings are given in Appendix 9 of this RAP

PK samples collected outside the protocol defined time-windows and/or other protocol deviations will be reviewed by the study team to determine whether the sample will be excluded from PK analyses. PK reporting will also consider planned Quality Tolerance Limit (QTL) outcomes affecting study data quality. Details are found in the QTL Report.

8.4. Strategy for Intercurrent Events – Covid-19 Complications

While incidents of Covid-19 could be expected to affect subject safety, its effect on CAB + RPV PK concentrations is unknown. Given the small study sample size implying less likelihood that a subject acquires Covid-19 through the course of the study, the benefit of a sensitivity analysis for subjects that acquire Covid-19 during the course of their PK sampling appears minimal. Should more information become available and/or the clinical need arise, this RAP may be amended to include Covid-19 PK sensitivity analyses in order to further understand any potential interacting effects.

9. HEALTH OUTCOMES ANALYSES

Health outcomes questionnaire data will be summarised and listed by, or under the direct auspices of, Clinical Statistics, GlaxoSmithKline. The health outcomes analyses will be based on the Safety population, unless otherwise specified. All questionnaire data will be listed by subject, item, treatment, and timepoint as applicable.

No formal statistical analysis of the health outcomes data will be conducted. The precise format and content of health outcomes tables and listings are shown in Appendix 5 of the RAP.

CCI

10. REFERENCES

GlaxoSmithKline Document Number 2018N357118_00: A Phase 1, Multicompartment Pharmacokinetic Study of Cabotegravir Long-acting in Healthy Adult Volunteers. Effective Date: 02-MAR-2020

GlaxoSmithKline Document Number 2018N357118_01: A Phase 1, Multicompartment Pharmacokinetic Study of Cabotegravir Long-acting in Healthy Adult Volunteers. Effective Date: 13-AUG-2020

GlaxoSmithKline Document: Covid-19 Guidance for Estimands and Estimation.

GlaxoSmithKline Document: Impact of Covid-19 on Assessment of Safety in Clinical Trials.

11. APPENDICIES

11.1. Appendix 1: Schedule of Activities

11.1.1. Screening and Oral Lead-in Phase

Study Period	**Screening[1]**		**Oral Lead-in[9]**			**Day 29**	**Early Withdrawal[9]**	**Washout Period**
			Dosing Days 1-28					
Visit Window	**Within 30 days of oral lead-in**	**Day -1**	**Day 1**	**Day 2**	**Day 14**	**Within 24 hours of the Day 28 last dose**	**EW**	**10 – 14 days**
Informed Consent	X							
Demographics	X							
Medical / Medication / Drug / Alcohol History	X							
Inclusion/Exclusion Criteria[2]	X		X					
Height, Weight, BMI	X							
Physical Exam	X		X					
Vital Signs[3]	X		X	X	X	X	X	
12-Lead ECG	X		X			X		
Drug / Alcohol Screen[3]	X		X					
Pregnancy Test[3]	X		X		X	X		
Testing for SARS-CoV-2[4]	X	X						
Hepatitis B, Hepatitis C Screening	X							
HIV Test	X							
Urine Dipstick	X							
Hematology with differential; Clinical Chemistry Tests[3]	X		X	X	X	X	X	
Coagulation Tests	X							
Admit to clinic		X						
Dispense Oral lead-in IP			X					

Study Period	Screening[1]		Oral Lead-in[9]			Day 29	Early Withdrawal[9]	Washout Period
			Dosing Days 1-28					
Visit Window	**Within 30 days of oral lead-in**	**Day -1**	**Day 1**	**Day 2**	**Day 14**	**Within 24 hours of the Day 28 last dose**	**EW**	**10 – 14 days**
Administer oral CAB + RPV[5]			X	X	X			
Dispense Medication Dosing Diary				X				
Drug accountability/ pill count/review drug diary				X	X	X		
Blood plasma PK sampling[6]			X	X	X	X	X	
AE Assessment[7]			X	X	X	X	X	
Concomitant Medication Review			X	X	X	X	X	
Genetic sample[8]			X					
Discharge from the clinic				X				

1. Screening may occur over more than one visit but within 30 days of the first dose of oral CAB and RPV in the oral lead in phase.
2. Eligibility criteria must be carefully assessed at the Screening visit and confirmed at the Day 1 Oral lead-in phase visit and re-confirmed prior to injection.
3. Prior to administering the first oral dose of CAB and RPV, study personnel must verify the following pre-dose assessments to be within normal limits prior to administration: vital signs, pregnancy test (negative; Females of Reproductive Potential (FRP) only. The results of the Drug/Alcohol screen, hematology with differential, and clinical chemistry tests on Day 1 are not required prior to administering the first oral doses of CAB and RPV but should be drawn prior to CAB and RPV administration.
4. Following the second test for SARS-CoV-2, participants will be advised to self-quarantine until entrance to the unit while awaiting final testing clearance.
5. Oral CAB and RPV dosing Days 1 to 28. Day 1, Day 2, and Day 14 doses should be administered in the clinic.
6. PK sampling – On Day 1 - 1h, 2h, 3h, 4h, 6h, 8h, and 12h, and Day 2 PK between 22-26 h from first oral dose. On Day 14 pre-dose samples. Day 29 assessments should occur between 22-26 hours from the last dose on Day 28. Total of 20 PK samples (10 for CAB, 10 for RPV assay) will be collected during oral lead-in phase. Please refer to Protocol Section 8.4 for permitted PK window for OLI phase.
7. AE assessment will include a brief, symptom-directed physical exam as needed.
8. Genetic sample - collect the sample at the earliest convenient time after the first dose in the oral lead in phase on Day 1.
9. If a participant is withdrawn prior to receiving the CAB LA and/or RPV LA injection, a follow-up/withdrawal visit should be scheduled 10-14 days after the last oral dose of CAB and RPV.

11.1.2. CAB LA + RPV LA Injection Phase and Follow- up

Procedures	Injection Phase											Follow-up						
	Injection Day 1			Day 2	Day 4	Day 5	Day 7/8	Day 10	Day 15	Day 17	Day 22	Day 28 (Week 4)	Week 8	Week 12	Week 24	Week 36	Week 52	Withdrawal[1]
	Pre-dose[2]	1h	2h	24h	72h	96h	168h											
Permitted window for PK collection	Within 1 h prior to dosing	± 15 min	± 30 min	± 2 h	± 2 h	± 2 h	± 2 h	± 2 h	± 2 h	± 2 h	± 2 h	± 2 h	± 3 days	± 3 days	± 3 days	± 3 days	± 3 days	
Interim Medical/Medication/ Drug / Alcohol History[2]	X																	
Pregnancy Test	X											X	X	X	X	X	X	X
12-Lead ECG[2]	X		X			X											X	X
HIV Test	X														X		X	X
Testing for SARS-CoV-2																		
Hematology; Clinical Chemistry	X						X			X		X	X	X	X	X	X	X
Vital Signs[2]	X			X		X	X	X	X	X	X	X	X	X	X	X	X	X
Administer CAB LA + RPV LA[2]	X																	
CCI		X[3]		X[3]	X[3]	X[3]	X[3]											
							X[3]											
Injection site reaction assessment		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
AE Assessment[4]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medication Review	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Blood plasma PK Sampling[5]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

1. Participants who terminate before week 52 will be asked to return to the site for a withdrawal visit.
2. On Day 1, study personnel must verify the following pre-dose assessments to be within normal limits prior to injection: ECG, vital signs, pregnancy test (negative; FRP only), review AE assessment, and concomitant medications. If a clinical abnormality, clinically significant AE, or prohibited medication that precludes injection is observed/recorded, the medical monitor must be contacted for further instruction.
3. Participants will be asked to describe the comfort level with the injections received. CCI [redacted] CCI
4. AE assessment will include a brief, symptom-directed physical exam as needed.
5. Total of 34 PK samples (17 each for CAB and RPV) will be collected through CAB LA + RPV LA Injection Phase and Follow-up.

11.2. Appendix 2: Assessment Windows

All assessments/events (including those from planned, unscheduled and withdrawal visits) will be assigned to assessment windows/analysis visits according to actual dates of collection rather than the nominal visit labels recorded on the eCRF or in the laboratory database. All assessment data, including unscheduled data will be presented in listings.

For parameters which are not scheduled to be assessed at a particular visit, the all-inclusive assessment windows will still be used; however, data displays summarizing measurements by visit will only report visits in which the parameter is a planned collection according to Appendix 1: Schedule of Activities

Note: Prior to visit slotting, assessments are first assigned to a study phase according to Table 3.

11.2.1. Definitions of Assessment Windows

Table 8 Assessment Windows for Screening and OLI Phase Data

Parameter	Analysis Window	Target Period Day	Analysis Timepoint
Assessments assigned to Phase=Screening or OLI (per Table 3)			
All	OLI Phase Day <1	The day of earliest record	Screening
PK, Vital Signs, Labs, ECG	OLI Phase Day = 1	1	Day 1
PK, Vital Signs, Labs	OLI Period Day = 2	2	Day 2
PK	13 ≤ OLI Phase Day ≤ 15	14	Day 14
Vital Signs, Labs	3 ≤ OLI Phase Day ≤ 21	14	Day 14
PK	28 ≤ OLI Phase Day ≤ 30	29	Day 29
Vital Signs, Labs, ECG	22 ≤ OLI Phase Day	29	Day 29
If none of the above			Day X, where X=OLI Phase day

Table 9 Assessment Windows for Injection & Follow-up Phase Data

Parameter [a]	Analysis Window	Target Period Day	Analysis Timepoint
Assessments assigned to Phase=Injection (per Table 3)			
PK, Vital Signs, Labs, ECG, CCI	Injection Phase Day = 1	1	Day 1
PK, Vital Signs, CCI	Injection Phase Day = 2	2	Day 2
PK	Injection Phase Day = 4	4	Day 4
CCI	3 ≤ Injection Phase Day ≤ 4	4	Day 4
PK	Injection Phase Day = 5	5	Day 5
Vital Signs	3 ≤ Injection Phase Day ≤ 6	5	Day 5
CCI	5 ≤ Injection Phase Day ≤ 6	5	Day 5
ECG	2 ≤ Injection Phase Day	5	Day 5

Parameter [a]	Analysis Window	Target Period Day	Analysis Timepoint
PK	Injection Phase Day = 7	7	Day 7
PK	Injection Phase Day = 8	8	Day 8
CCI	7 ≤ Injection Phase Day	8	Day 8
Vital Signs	7 ≤ Injection Phase Day ≤ 9	8	Day 8
Labs	2 ≤ Injection Phase Day ≤ 10	8	Day 8
PK	Injection Phase Day = 10	10	Day 10
Vitals	10 ≤ Injection Phase Day ≤ 12	10	Day 10
PK	Injection Phase Day = 15	14	Day 15
Vital Signs	12 ≤ Injection Phase Day ≤ 16	14	Day 15
PK	Injection Phase Day = 17	17	Day 17
Vital Signs	17 ≤ Injection Phase Day ≤ 19	17	Day 17
Labs	11 ≤ Injection Phase Day ≤ 23	17	Day 17
PK	Injection Phase Day = 22	22	Day 22
Vital Signs	20 ≤ Injection Phase Day ≤ 25	22	Day 22
PK	Injection Phase Day = 28	28	Week 4
Vital Signs	26 ≤ Injection Phase Day	28	Week 4
Labs	24 ≤ Injection Phase Day	28	Week 4
	If none of the above		Day X, where X=Injection Phase Day
Assessments assigned to Phase=Follow-up (per Table 3)			
Vital Signs, Labs	(Date of Nominal Follow-up Week 4 Visit – CAB + RPV Injection Date) +2 ≤ Injection Phase Day ≤ 70	56	Week 8
PK	53 ≤ Follow-up Period Day ≤ 59	56	Week 8
Vital Signs, Labs	71 ≤ Follow-up Period Day ≤ 126	84	Week 12
PK	81 ≤ Follow-up Period Day ≤ 87	84	Week 12
Vital Signs, Labs	127 ≤ Follow-up Period Day ≤ 210	168	Week 24
PK	165 ≤ Follow-up Period Day ≤ 171	168	Week 24
Vital Signs, Labs	211 ≤ Follow-up Period Day ≤ 308	252	Week 36
PK	249 ≤ Follow-up Period Day ≤ 255	252	Week 36
Vital Signs, Labs, ECG	309 ≤ Follow-up Period Day	364	Week 52
PK	361 ≤ Follow-up Period Day ≤ 367	364	Week 52
If none of the above			Day X, where X=Follow-up Phase Day

NOTES:

- OLI Day, Injection Day, and Follow-up Day are defined in Section 11.5.1.

11.3. Appendix 3: Study Phases and Treatment Emergent Adverse Events

11.3.1. Study Phases

All assessments and events (including those collected as planned, early withdrawal and unscheduled visits) will be classified in study phases according to Table 3.

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

Table 3 Assignment of Study Phases

For All Events or Assessments	
Study Period	**Date range**
Screen	**If actual "Time of Day" for the assessment/event is collected:**
	Start Date and Time < OLI Treatment Start Date & Time
	If actual "Time of Day" for the assessment/event is not collected:
	Start Date < OLI Treatment Start Date
OLI Phase	**If actual "Time of Day" for the assessment/event is collected:**
	For participants continuing into Injection Phase: OLI Treatment Start Date & Time ≤ **Start Date & Time** < Date & Time of CAB + RPV Injection **For participants not continuing into Injection Phase:** OLI Treatment Start Date & Time ≤ **Start Date & Time**
	If actual "Time of Day" for the assessment/event is not collected:
	For participants continuing into Injection Phase: OLI Treatment Start Date ≤ **Start Date** < Date of CAB + RPV Injection **For participants not continuing into Injection Phase:** OLI Treatment Start Date ≤ **Start Date**
Injection Phase	**If actual "Time of Day" for the assessment/event is collected:**
	Date & Time of CAB + RPV Injection ≤ **Start Date & Time** and **Start Date** ≤ Date of Nominal Follow-up Week 4
	If actual "Time of Day" for the assessment/event is not collected:
	Date of CAB + RPV Injection ≤ **Start Date** ≤ Date of Nominal Follow-up Week 4 Visit
Follow-up Phase	Date of Nominal Follow-up Week 4 Visit < **Start Date**

NOTES:

- Date = Date of assessment

Table 4 Study Phases for Concomitant Medication

Concomitant during:	
Study Period	**Date range**
Prior	**Medication Taken** < OLI Treatment Start Date & Time
OLI Phase	**For participants continuing into Injection Phase:** OLI Treatment Start Date & Time ≤ **Medication Taken** < Injection Phase Treatment Start Date & Time **For participants not continuing into Injection Phase:** OLI Treatment Start Date & Time ≤ **Medication Taken**
Injection Phase	Injection Phase Treatment Start Date & Time ≤ **Medication Taken** ≤ Date of Nominal Follow-up Week 4 Visit
Follow-Up Phase	Date of Nominal Follow-up Week 4 Visit < **Medication Taken**

NOTES:

- If concomitant medication time is missing, the medication will be assumed to be taken predose, prior to that day's treatment dosing.
- Please refer to Appendix 6: Reporting Standards for Missing Data. for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

11.3.2. Treatment Emergent Flag for Adverse Events

Flag	**Definition**
Treatment Emergent	• AEs will be considered emergent in the OLI, Injection and Follow-up Phases according to the classification defined in Table 3. AEs that occur in the Follow-up Phase will be considered Treatment Emergent.

11.4. Appendix 4: Data Display Standards and Handling Conventions

11.4.1. Reporting Process

Software	
• The currently supported versions of SAS software version 9.4 will be used.	
Reporting Area	
HARP Server	us1salx00259
HARP Compound	\ARPROD\GSK1265744\mid213199\internal_01 \ARPROD\GSK1265744\mid213199\internal_02 \ARPROD\GSK1265744\mid213199\primary_01
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1.	
Generation of RTF Files	
• RTF files will be generated for all tables in Appendix 9: List of Data Displays.	

11.4.2. Reporting Standards

General

• The current GSK Statistical Display Standards in the GSK Standards Library (IDSL) will be applied for reporting, unless otherwise stated (Library 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 Statistical Display 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 GSK Standard Statistical Display Principles but may be adjusted to a clinically interpretable number of DP's.
Planned and Actual Time

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

Unscheduled Visits	
• Unscheduled visits will be assigned to a study visit using assessment windows defined in Section 11.2.1. • However, data summaries will only report visits that are planned assessment time points for each parameter (according to the Schedule of Activities in Section 11.1). • Evaluable assessments at unscheduled visits will be used when categorizing values across visits, such as 'maximum grade during the injection phase'.	
Descriptive Summary Statistics	
Continuous Data	Refer to GSK Standard Statistical Display Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to GSK Standard Statistical Display Principals 7.01 to 7.13.	

11.4.3. Reporting Standards for Pharmacokinetic Data

Pharmacokinetic Concentration Data	

Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards.
	Refer to IDSL Statistical Principle 6.06.1.
	For continuous data:
	• Not quantifiable values (NQs) at the beginning of a participant profile (i.e. before the first incidence of a measurable concentration) are deemed to be zero as it is assumed that in this circumstance no drug is yet measurable in the blood.
	• For NQs at the end of the participant profile (i.e. after the last incidence of a measurable concentration);
	  • for individual plots and pharmacokinetic analyses these are dropped (set to missing) as they do not provide any useful information (and can erroneously indicate that absolutely no drug is present)
	  • for summary statistics, these are set to 0 (to avoid skewing of the summary statistics)
	• Individual NQs which fall between two measurable concentrations are set to missing (individual values of this nature are assumed to be an anomaly).
	  • If two or more NQ values occur in succession between measurable concentrations, the profile will be deemed to have terminated at the last measurable concentration prior to these NQs. For the purpose of individual participant plots, these NQs will be set to 0, and the subsequent measurable concentrations will be retained. For the derivation of pharmacokinetic parameters, these NQs and any subsequent measurable concentrations will be omitted (set to missing).
	Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.

11.4.4. Reporting Standards for Liver Safety Data

11.4.4.1. Liver Stopping/Monitoring Criteria

Element	Reporting Detail
General	• A liver monitoring event occurs when subject meets predefined liver chemistry monitoring criteria that trigger increased monitoring of the subject's liver chemistries, but no action is taken with study treatment unless liver chemistry stopping criteria are

Element	Reporting Detail
	met. A liver stopping event occurs when subject meets predefined liver chemistry stopping criteria, ALT >=3xULN for this study, that trigger discontinuation of study treatment and requirement of additional actions and follow up assessments to be performed. For subjects with more than one liver stopping or liver monitoring event, only data related to the earliest most severe criteria event is included in displays. • Resolved is defined as ALT <3xULN for 2 consecutive visits or <3xULN for one visit if subject discontinued and no data available. Post treatment records are included to evaluate resolution of the event.

11.4.4.2. Hepatobiliary Abnormality Criteria

Element	Reporting Detail
General	• To include ALT, ALP, Bilirubin, & INR parameters
ALT >=3xULN and BIL >=2xULN	• If direct bilirubin is available (on the same date as Total Bilirubin), then direct bilirubin as a portion of total bilirubin must be >=35% when total bilirubin is >=2xULN, in order to satisfy the criteria. • Bilirubin value is on or up to 28 days after ALT value.
ALT >=3xULN and INR >1.5	• INR value is on or up to 28 days after ALT value.
ALT >=3xULN and BIL >=2xULN and ALP 2 (<1%) <2xULN	• If direct bilirubin is available (on the same date as Total Bilirubin), then direct bilirubin as a portion of total bilirubin must be >=35% when total bilirubin is >=2xULN, in order to satisfy the criteria. • Bilirubin value is on or up to 28 days after ALT value. • The ALP value must occur on or up to 28 days after the ALT value.
Hepatocellular injury	• Hepatocellular injury is defined as ((ALT/ALT ULN)/(ALP/ALP ULN)) >=5 and ALT >=3xULN. ALT and ALP values must occur on the same day.
Hepatocellular injury and BIL >=2xULN	• Hepatocellular injury is defined as ((ALT/ALT ULN)/(ALP/ALP ULN)) >=5 and ALT >=3xULN. ALT and ALP values must occur on the same day. • If direct bilirubin is available (on the same date as Total Bilirubin), then direct bilirubin as a portion of total bilirubin must be >=35% when total bilirubin is >=2xULN, in order to satisfy the criteria. • Bilirubin value is on or up to 28 days after ALT value.
BIL >=2xULN	• If direct bilirubin is available (on the same date as Total Bilirubin), then direct bilirubin as a portion of total bilirubin must be >=35% when total bilirubin is >=2xULN, in order to satisfy the criteria.
AST >3xULN and ALP <2xULN and BIL >=2xULN	• ALP and BIL values must occur on or up to 28 days after AST value. • If direct bilirubin is available (on the same date as Total Bilirubin), then direct bilirubin as a portion of total bilirubin must be >=35% when total bilirubin is >=2xULN, in order to satisfy the criteria.

Element	Reporting Detail
ALT>=X ULN and AST>=X ULN	• AST and ALT values must occur on the same day

11.5. Appendix 5: Derived and Transformed Data

11.5.1. General

Multiple Measurements at One Analysis Time Point
• If there are multiple measurements within a time window (per Section 11.2.1), the value closest to the target day for that window will be used. If values are the same distance from the target, then the mean of the measurements (for quantitative parameters including ECG values) or the worst-case of the measurements (for qualitative parameters) will be calculated and used in any derivation of summary statistics. • Only planned assessment timepoints (according to Appendix 2: Schedule of Activities) will be included in data displays summarizing measurements by visit. • Assessments not chosen for use in summary statistics will still appear in the associated listings. • All applicable valid assessments, irrespective of proximity to the target study day, will be used when categorizing values across visits, such as 'maximum grade during the intervention phase' or 'at any time post-baseline', and for any algorithm that has specific rules for which observation to use (e.g. LOCF).
Change from Baseline
• Post-Dose Visit Value – Baseline • Unless otherwise specified, the baseline definitions specified in Section 6.2 will be used for derivations for endpoints / parameters.
Study Day

• The Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE) will be derived as the number of days between the date of the event and the Intervention Phase treatment start date as follows:
  ○ If date of event ≥ start date of study treatment, then
  ▪ Study Day = Date of Event - Intervention Phase Treatment Start Date +1
  ○ If date of event < start date of study treatment, then
  ▪ Study Day = Date of Event - Intervention Phase Treatment Start Date
  ○ Note that the start date of each phase is on Study Day 1 and the day before this is Study Day -1; i.e., there is no Study Day 0.

Phase Day
• Calculated as the number of days from First Dose Date of CAB + RPV for the respective phase (based on study period classifications in Table 3): OLI phase: • If Assessment Date < First Dose Date of Oral CAB + RPV then • Phase Day = Assessment Date – First Dose Date of Oral CAB + RPV • If Assessment Date ≥ First Dose Date of Oral CAB + RPV then • Phase Day = Assessment Date – First Dose Date of Oral CAB + RPV +1 Injection phase: • If Assessment Date < Dose Date of Injection CAB + RPV then • Phase Day = Assessment Date – Dose Date of Injection CAB + RPV • If Assessment Date ≥ Dose Date of Injection CAB +RPV then • Phase Day = Assessment Date – Dose Date of Injection CAB + RPV +1 Follow-up phase: • If Assessment Date < Follow-up Week 4 Visit Date then • Phase Day = Assessment Date – Follow-up Week 4 Visit Date • If Assessment Date ≥ Follow-up Week 4 Visit Date then • Phase Day = Assessment Date – Follow-up Week 4 Visit Date +1

11.5.2. Study Population

Age
• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows: ○ Any participant with a missing day will have this imputed as day '15'. ○ Any participant with a missing day and month will have this imputed as '30th June'. • Birth date will be presented in listings as 'YYYY'. • Completely missing dates of birth will remain as missing, with no imputation applied. Consequently, the age of the subject will not be calculated and will remain missing.
Body Mass Index (BMI)
• Calculated in the CRF as Weight (kg) / [Height $(m)^2$]

11.5.3. Safety

Exposure

Compliance

Compliance for the OLI Phase will be calculated as follows:

$$\text{OLI Compliance \%} = \frac{\#\ days\ subject\ took\ the\ study\ drug}{Minimum\ (\#\ of\ days\ subject\ was\ enrolled\ in\ the\ OLI\ period, 28)}$$

Extent of Exposure

- Exposure to CAB+RPV Oral Lead-in = IP (oral lead-in) stop date - IP (oral lead-in) start date +1

Duration (Days)

- AE Resolution Date – AE Start Date + 1

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

12-Lead Electrocardiograms

QTcB Interval

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

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

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

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.,

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

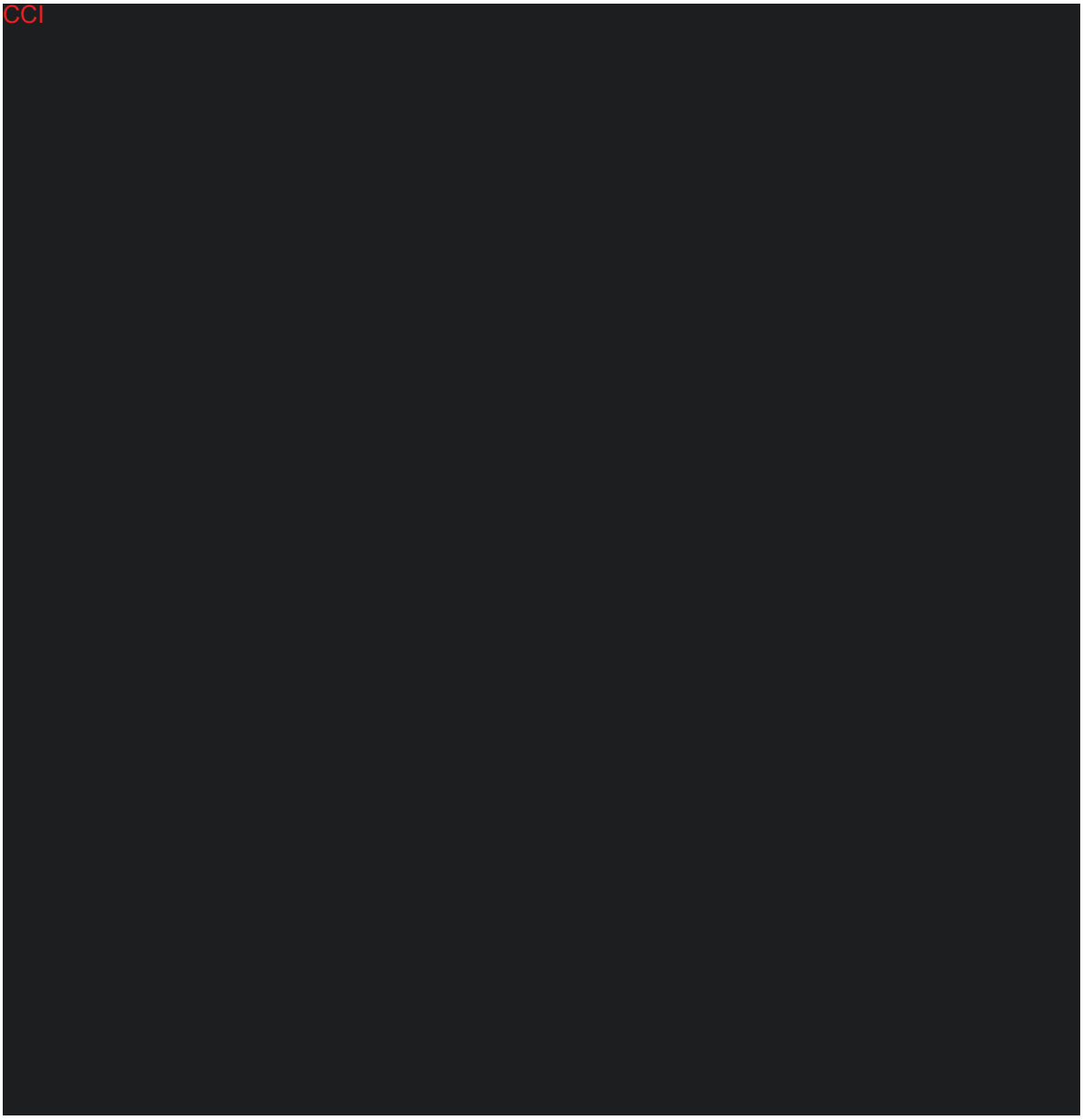
11.5.4. Pharmacokinetic

Pharmacokinetic Parameter Statistics

• For the purposes of calculating summary statistics and for statistical analysis, all PK parameters with the exception of t_{max} will be log_e transformed.
• Geometric coefficient of variation:
  ○ Untransformed Data: 100 * (SD/Mean).
  ○ Transformed Data: 100 * (sqrt(exp(SD_{log}^2)-1)) where SD_{log} indicates the standard deviation of log-transformed data

11.5.5. Health Outcomes

CCI



CCI

11.6. Appendix 6: Reporting Standards for Missing Data

11.6.1. Premature Withdrawals

Element	Reporting Detail
General	• Withdrawn participants may be replaced in the study. All subjects who withdraw prematurely from the study/study drug will be documented and the reason for their withdrawal recorded in the final Clinical Pharmacology Study Report (CPSR). • 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 according to Appendix 2: Assessment Windows

11.6.2. 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.
CCI	• Subjects who were injected that have missing CCI data may have it imputed with their last observation carried forward (LOCF)

11.6.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays. • Where necessary, partial dates may be imputed for specific analysis purposes as outlined below. • Imputed partial dates will not be used to derive study day, time to onset or duration (e.g., time to onset or duration of AEs), or elapsed time variables (e.g., time since diagnosis).
Adverse Events	• Imputations in the AEs dataset are used for slotting events to the appropriate study time periods and for sorting in data listings. • Partial dates for AE recorded in the eCRF will be imputed using the following conventions: Missing start day: • If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = 1st of month. • Else if study treatment start date is not missing: ○ If month and year of start date = month and year of study treatment start date then ▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date= 1st of month.

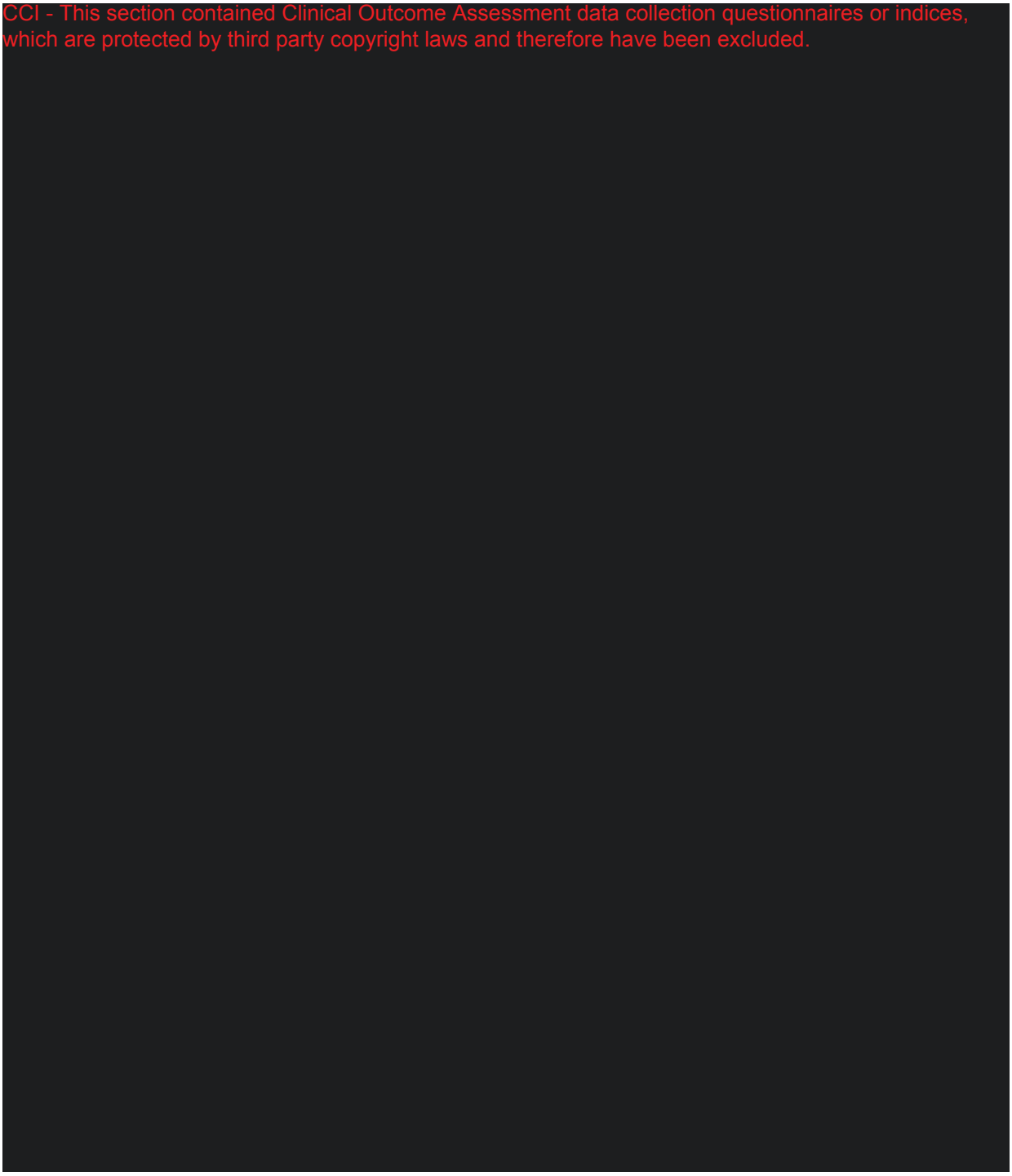
<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
<tr><td></td><td>
<table>
<tr><td></td><td>▪ Else set start date = study treatment start date.
○ Else set start date = 1st of month.</td></tr>
<tr><td>Missing start day and month</td><td>• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = January 1.
• Else if study treatment start date is not missing:
○ If year of start date = year of study treatment start date then
▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date = January 1.
▪ Else set start date = study treatment start date.
○ Else set start date = January 1.</td></tr>
<tr><td>Missing stop day</td><td>Last day of the month will be used.</td></tr>
<tr><td>Missing stop day and month</td><td>No Imputation</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table>
• Completely missing start or end dates will remain missing, with no imputation applied.
</td></tr>
<tr><td>Concomitant Medications</td><td>
• Partial dates for any concomitant medications recorded in the eCRF will be imputed using the following convention:
<table>
<tr><td>Missing start day</td><td>• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = 1st of month.
• Else if study treatment start date is not missing:
○ If month and year of start date = month and year of study treatment start date then
▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date= 1st of month.
▪ Else set start date = study treatment start date.
○ Else set start date = 1st of month.</td></tr>
<tr><td>Missing start day and month</td><td>• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = January 1.
• Else if study treatment start date is not missing:
○ If year of start date = year of study treatment start date then
▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date = January 1.
▪ Else set start date = study treatment start date.
• Else set start date = January 1.</td></tr>
<tr><td>Missing end day</td><td>A '28/29/30/31' will be used for the day (dependent on the month and year)</td></tr>
<tr><td>Missing end day and month</td><td>A '31' will be used for the day and 'Dec' will be used for the month.</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table>
• The recorded partial date will be displayed in listings.
</td></tr>
</table>

11.7. Appendix 7: Values of Potential Clinical Importance

11.7.1. Laboratory Values

Laboratory values 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 11.7, and shown below:

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



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

11.7.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec	<320	>450
Absolute PR Interval	msec	<120	>220
Absolute QRS Interval	msec	<70	>120
Change from Baseline			
Increase from Baseline QTc	msec		>60

11.8. Appendix 8: Abbreviations & Trademarks

11.8.1. Abbreviations

ADaM	Analysis data model
AE	Adverse event
ALT	alanine aminotransferase (SGPT)
AST	Aspartate aminotransferase (SGOT)
ATC	Anatomical Therapeutic Chemical Classification level
AUC_{0-t}	Area under the concentration time curve from time zero to last quantifiable time point
$AUC_{0-\tau}$	Area under the concentration-time curve over one dosing interval
$AUC_{0-\infty}$	Area under the concentration time curve from time zero to infinity
AUC_{0-24}	Area under the concentration-time curve over 24 hours
BMI	Body mass index
BQL	Below the quantification limit
CAB	Cabotegravir
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence interval
C_{max}	Maximum observed concentration
CPK	Creatine phosphokinase
CPMS	Clinical Pharmacokinetic Modelling Simulation
C24	Concentration at 24-hour timepoint
$C\tau$	Last observed quantifiable concentration
CV	Coefficient of variance
CV_b	Geometric Coefficient of variation
ECG	Electrocardiogram
GSK	GlaxoSmithKline
HIV	Human immunodeficiency virus
HO	Health Outcomes
IDSL	Integrated Data Standards Library
IM	Intramuscular
IP	Investigational product
ISR	Injection site reaction
K_A LA	Absorption rate constant, Long-acting
λ_z	Terminal phase rate constant
LA	Long-acting
LOCF	Last Observation Carried Forward
MedDRA	Medical Dictionary for Regulatory Activities
Mg	Milligrams
mL	Milliliter
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NQ	Non-quantifiable
CCI	[redacted]

OLI	Oral Lead In
PK	Pharmacokinetic(s)
CCI [redacted]	
QTcB	QT duration corrected for heart rate by Bazett's formula
QTcF	QT duration corrected for heart rate by Fridericia's formula
RAP	Reporting and Analysis Plan
RPV	Rilpivirine
SAE	Serious adverse event(s)
SAS	Statistical Analysis Software
SD	Standard deviation
SDTM	Study Data Tabulation Model
SoA	Schedule of Activities
SOP	Standard operating procedure
$t_{½}$	Apparent terminal phase half-life
τ	Dosing interval
t_{max}	Time of occurrence of Cmax
ULN	Upper limit of normal

11.8.2. Trademarks

Trademarks of ViiV Healthcare
NONE

Trademarks not owned by ViiV Healthcare
MedDRA
SAS
Winnonlin

11.9. Appendix 9: List of Data Displays

All data displays will use the term "subject" rather than "participant" in accordance with CDSIC and GSK Statistical Display Standards.

The list of data displays included in this critical component RAP is tentative, to be confirmed and modified as appropriate during the development of the full RAP.

11.9.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.10	N/A
Safety	3.1 to 3.37	3.38
Pharmacokinetic	4.1 to 4.4	4.5 to 4.10
Health Outcomes	6.1 to 6.7	N/A
Section	**Listings**	
ICH Listings	1 to 24	
Other Listings	25 to 38	

11.9.2. Deliverables

Delivery	Description
Interim	Informal Interim PK Analyses at Week 4 and Week 12 post injection
SAC	Final Statistical Analysis Complete

11.9.3. Study Population Tables

Study Population Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Safety	ES1	Summary of Subject Disposition for the Subject Conclusion Record	ICH E3, FDAAA, EudraCT	SAC
1.2.	Safety	DISP_T1	Summary of Subject Disposition at Each Study Phase	ICH E3	SAC
1.3.	Safety	DISP_T2	Summary of Reasons for Withdrawal at Each Study Phase		SAC
1.4.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements	SAC
Protocol Deviation					
1.5.	Safety	DV1	Summary of Important Protocol Deviations by Study Phase and Overall	ICH E3	SAC
Population Analysed					
1.6.	Enrolled	SP1	Summary of Study Populations by Study Phase and Overall	GSK Statistical Display Standard Note: Show n's at each study phase.	SAC
Demographic and Baseline Characteristics					
1.7.	Safety	DM1	Summary of Demographics and Baseline Characteristics	ICH E3, FDAAA, EudraCT Note: To include Age Ranges	SAC
1.8.	Safety	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT	SAC
Prior and Concomitant Medications					
1.9.	Safety	MH1	Summary of Past Medical Conditions	ICH E3	SAC
1.10.	Safety	CM1	Summary of Concomitant Medications by Study Phase and Overall	ICH E3	SAC

11.9.4. Safety Tables

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure and Treatment Compliance					
3.1.	Safety	207966/primary_15/ T3.1	Summary of Exposure to Study Treatment	ICH E3 Display treatment in columns. Include the following parameters: "Exposure (Days-oral lead-in)" "Exposure (Weeks-oral lead-in)" "Oral Lead-in Compliance %" from 11.5.3 "No. of Subjects Receiving Injections" "Number of Injections"	SAC
Adverse Events (AEs)					
3.2.	Safety	AE13	Adverse Event Overview by Study Phase and Overall	High level summary to include counts of overall AEs, Treatment emergent AEs, Serious AEs, AEs leading to withdrawal, related AEs, serious related AEs, AEs related to Covid-19, AEs related to Covid-19 leading to withdrawal, fatal AEs Repeat for each study phase and overall	SAC
3.3.	Safety	AE1xo	Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3	SAC
3.4.	Safety	AE5B	Summary of All Adverse Events by System Organ Class, Preferred Term, and Maximum Grade	ICH E3 Repeat for each study phase and overall	SAC

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.5.	Safety	AE15	Summary of Common (>=10%) Adverse Events by Overall Frequency (Number of Subjects and Occurrences)	ICH E3 Note: "Common" AEs will be based on the Total column. Repeat for each study phase and overall	SAC
3.6.	Safety	AE5B	Summary of Common (>=10%) Adverse Events by System Organ Class, Preferred Term, and Maximum Grade	ICH E3 Note: "Common" AEs will be based on the Total column. Repeat for each study phase and overall	SAC
3.7.	Safety	AE5B	Summary of Drug-Related Adverse Events by System Organ Class, Preferred Term, and Maximum Grade	ICH E3 Repeat for each study phase and overall	SAC
3.8.	Safety	AE15	Summary of Common (>=10%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT Note: "Common" AEs will be based on the Total column. Repeat for each study phase and overall	SAC
Serious and Other Significant Adverse Events					
3.9.	Safety	AE5B	Summary of Serious Adverse Events by System Organ Class, Preferred Term, and Maximum Grade	ICH E3 Repeat for each study phase and overall	SAC
3.10.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT Repeat for each study phase and overall	SAC

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.11.	Safety	AE5B	Summary of Serious, Drug-Related Adverse Events by System Organ Class, Preferred Term, and Maximum Grade	Repeat for each study phase and overall	SAC
3.12.	Safety	AE5B	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class, Preferred Term, and Maximum Grade	GSK Statistical Display Standard Repeat for each study phase and overall	SAC
3.13.	Safety	AE5B	Summary of All Drug-Related Adverse Events Excluding Injection Site Reactions by System Organ Class, Preferred Term, and Maximum Grade	Repeat for each study phase and overall	SAC
3.14.	Safety	PAN1A	Summary of COVID-19 Assessments for Subjects with COVID-19 Adverse Events	Note: To also include results of Covid-19 tests performed	SAC
3.15.	Safety	AE5B	Summary of Covid-19 Adverse Events by System Organ Class, Preferred Term, and Maximum Grade	Repeat for each study phase and overall	SAC
3.16.	Safety	AE1xo	Summary of Covid-19 Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term	Repeat for each study phase and overall	SAC
3.17.	Safety	AE15	Summary of Serious Covid-19 Adverse Events by System Organ Class, and Preferred Term (Number of Subjects and Occurrences)	Repeat for each study phase and overall	SAC
3.18.	Safety	PAN3A	Summary of Covid-19 Symptoms for Subjects with COVID-19 Adverse Events	Note: data collected from AE_covid-19 eCRF	SAC
3.19.	Safety	PAN10A	Incidence of Covid-19 Adverse Events by Gender and Pandemic Course	Pandemic course = During and Post pandemic Post pandemic date to be provided upon availability.	SAC

Injection Site Reaction Adverse Events					
3.20.	Safety	201584/primary_7/T 3.43	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events by Treatment and Overall	Treatment to be listed in the columns	SAC
3.21.	Safety	201584/primary_7/T 3.40	Summary of Injection Site Reaction Adverse Events (Event-Level Summary) by Treatment and Overall	Treatment to be listed in the columns	SAC
3.22.	Safety	201584/primary_7/T 3.46	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events by Maximum Grade, Treatment, and Overall	Treatment to be listed in the columns	SAC
Adverse Events of Special Interest					
3.23.	Safety	201584/primary_07/ T3.134	Summary of Seizure Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC
3.24.	Safety	201584/primary_07/ T3.137	Summary of Hepatic Safety Profile: Assessment of Risk of Hepatotoxicity Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC
Laboratory: Chemistry					
3.25.	Safety	LB1	Summary of Chemistry Changes from Baseline by Study Phase and Visit	ICH E3	SAC
3.26.	Safety	LB1	Summary of Chemistry Values by Study Phase and Visit	ICH E3	SAC
3.27.	Safety	LB16	Summary of Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline	ICH E3 Repeat for each study phase	SAC
Laboratory: Hematology					
3.28.	Safety	LB1	Summary of Hematology Changes from Baseline by Study Phase and Visit	ICH E3	SAC
3.29.	Safety	LB1	Summary of Hematology Values by Study Phase and Visit	ICH E3	SAC
3.30.	Safety	LB16	Summary of Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline	ICH E3 Repeat for each study phase	SAC

Laboratory: Urinalysis					
3.31.	Safety	UR1	Summary of Worst-Case Urinalysis Results (Discrete or Character Values) Post-Baseline Relative to Baseline by Study Phase	ICH E3 Note: Define change categories according to actual values expected from lab dataset Repeat for each study phase and overall	SAC
Laboratory: Hepatobiliary (Liver)					
3.32.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting by Study Phase and Overall	GSK Statistical Display Standard Note: See Appendix 11.4.4 for Criteria	SAC
3.33.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities by Study Phase and Overall	GSK Statistical Display Standard Note: See Appendix 11.4.4 for Criteria	SAC
ECG					
3.34.	Safety	EG2	Summary of Change from Baseline in ECG Values by Study Phase and Visit	GSK Statistical Display Standard	SAC
3.35.	Safety	EG2	Summary of ECG Values by Study Phase and Visit	GSK Statistical Display Standard	SAC
3.36.	Safety	EG1	Summary of ECG Findings by Study Phase and Visit	GSK Statistical Display Standard	SAC
Vital Signs					
3.37.	Safety	VS1	Summary of Change from Baseline in Vital Signs by Study Phase and Visit	ICH E3	SAC

11.9.5. Safety Figures

Safety Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
3.38.	Safety	AE10	Plot of Common (>=10%) Adverse Events by Relative Risk, Study Phase, and Overall	Note: Display a different plot for each phase and overall	SAC

11.9.6. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetic Parameters					
4.1.	PK Parameter	PK_01	Summary of Derived Plasma Cabotegravir PK Parameters by Study Phase		Interim, SAC
4.2.	PK Parameter	PK_01	Summary of Derived Plasma Rilpivirine PK Parameters by Study Phase		Interim, SAC
Pharmacokinetic Concentration					
4.3.	PK Concentration	PK01	Summary of Plasma Cabotegravir PK Concentration (ug/mL)-Time Data by Study Phase and Nominal Timepoint		SAC
4.4.	PK Concentration	PK01	Summary of Plasma Rilpivirine PK Concentration (ng/mL)-Time Data by Study Phase and Nominal Timepoint		SAC

11.9.7. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetic Mean/Median Plots					
4.5.	PK Parameter	PK17	Mean (SD) Plasma Cabotegravir Concentration-Time Plots (Linear and Semi-Log) by Study Phase	Display oral and LA phases on separate pages	SAC
4.6.	PK Parameter	PK17	Mean (SD) Plasma Rilpivirine Concentration-Time Plots (Linear and Semi-Log) by Study Phase	Display oral and LA phases on separate pages	SAC
4.7.	PK Parameter	PK20	Median (5^{th} and 95^{th} Percentile) Plasma Cabotegravir Concentration-Time Plots (Linear and Semi-Log) by Study Phase	Display oral and LA phases on separate pages	SAC
4.8.	PK Parameter	PK20	Median (5^{th} and 95^{th} Percentile) Plasma Rilpivirine Concentration-Time Plots (Linear and Semi-Log) by Study Phase	Display oral and LA phases on separate pages	SAC
Pharmacokinetic Individual Subject Plots					
4.9.	PK Parameter	PK16a	Individual Plasma Cabotegravir Concentration-Time Plots (Linear and Semi-Log) by Study Phase	Display oral and LA phases on separate pages	SAC
4.10.	PK Parameter	PK16a	Individual Plasma Rilpivirine Concentration-Time Plots (Linear and Semi-Log) by Study Phase	Display oral and LA phases on separate pages	SAC

11.9.8. Health Outcomes Tables

Health Outcomes Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Questionnaire Outcomes					
6.1.	Safety	201584/primary_07/T6.2	CCI [redacted]		SAC
6.2.	Safety	201584/primary_07/T6.1			SAC
6.3.	Safety	201584/primary_07/T6.35			SAC
6.4.	Safety	201584/primary_07/T6.36			SAC
6.5.	Safety	201584/primary_07/T6.37			SAC
6.6.	Safety	201584/primary_07/T6.38			SAC
6.7.	Safety	201584/primary_07/T6.39			SAC

11.9.9. ICH Listings

ICH: Listings					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Screened	ES2	Listing of Reasons for Study Withdrawal	ICH E3	SAC
2.	Screened	SD2	Listing of Reasons for Study Treatment Discontinuation	ICH E3	SAC
Protocol Deviations					
3.	Screened	DV2	Listing of Protocol Deviations	ICH E3 Note: Include flag for important deviations (Y/N) and Covid-19 relatedness (Y/N)	SAC
4.	Screened	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	SAC
Populations Analysed					
5.	Screened	SP3	Listing of Subjects Excluded from Any Population	ICH E3	SAC
Demographic and Baseline Characteristics					
6.	Screened	DM2	Listing of Demographic Characteristics	ICH E3 Include column indicating inclusion in the enrolled (Y/N) and safety populations (Y/N)	SAC
7.	Screened	DM9	Listing of Race	ICH E3 Include column indicating inclusion in the enrolled (Y/N) and safety populations (Y/N)	SAC
Exposure and Treatment Compliance					
8.	Screened	EX3	Listing of Exposure Data	ICH E3	SAC

Adverse Events					
9.	Screened	AECP	Listing of All Adverse Events	ICH E3 Include column indicating Phase	SAC
10.	Screened	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3 Replace the column for treatment with Phase	SAC
11.	Screened	AECP	Listing of Serious Adverse Events	ICH E3 Include column indicating Phase Note: Include Fatal vs Non-Fatal Designation	SAC
12.	Screened	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	SAC
13.	Screened	AECP	Listing of Adverse Events Leading to Withdrawal from Study or Permanent Discontinuation of Study Treatment	ICH E3 Include column indicating Phase	SAC
14.	Screened	AECP	Listing of Covid-19 Adverse Events	ICH E3 Include column indicating Phase Note: Display Covid-19 Adverse events and descriptive details	SAC
15.	Screened	PAN12	Listing of COVID-19 Assessments and Symptom Assessments		SAC
16.	Screened	PAN5	Listing of Dates of COVID-19 Pandemic Measures	Include Pandemic End date if available	SAC
All Laboratory					
17.	Screened	LB5	Listing of Continuous Laboratory Data by Lab Category, Study Phase, and Visit	ICH E3 Note: Include Chemistry and Hematology results	SAC
18.	Screened	LB14	Listing of Categorical Laboratory Data by Lab Category, Study Phase, and Visit	ICH E3 Note: Include Urinalysis, Coagulation, Drugs, and Infectious Disease results	SAC
19.	Screened	EG3	Listing of ECG Values by Study Phase and Visit	Sort by Phase and Visit	SAC
20.	Screened	EG5	Listing of ECG Findings by Study Phase and Visit	Sort by Phase and Visit	SAC
21.	Screened	VS4	Listing of Vital Signs by Study Phase and Visit	Sort by Phase and Visit	SAC

22.	Screened	PREG1	Listing of Subjects Who Became Pregnant During the Study		SAC
PK					
23.	Screened	PK07	Listing of Plasma Cabotegravir PK Concentration-Time Data by study phase		SAC
24.	Screened	PK07	Listing of Plasma Rilpivirine PK Concentration-Time Data by study phase		SAC

11.9.10. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
25.	Screened	ES7	Listing of Reasons for Screen Failure	Journal Guidelines	SAC
26.	Screened	SD2	Listing of End of Study Record for Subjects Affected by Covid-19	Covid-19 relatedness as determined by Covid related AEs, PDs, missed visits, & Disposition	SAC
Prior and Concomitant Medications					
27.	Screened	MH2	Listing of Medical History for All Subjects		SAC
28.	Screened	CM3	Listing of Prior Medications	GSK Statistical Display Standard	SAC
29.	Screened	CM3	Listing of Concomitant Medications by Study Phase	GSK Statistical Display Standard	SAC
Adverse Events					
30.	Screened	AE8	Listing of Injection Site Reaction Adverse Events		SAC
31.	Screened	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	GSK Statistical Display Standard	SAC
Laboratory Results					
32.	Screened	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting	Note: See Appendix 11.4.4 for Criteria	SAC
33.	Screened	LIVER13	Listing Subjects Meeting Hepatobiliary Lab Abnormality Criteria	Note: See Appendix 11.4.4 for Criteria	SAC

PK					
34.	Screened	PK13	Listing of Derived Plasma Cabotegravir PK Parameters by study phase		SAC
35.	Screened	PK13	Listing of Derived Plasma Rilpivirine PK Parameters by study phase		SAC
Health Outcome					
36.	Screened	HO_01	Listing of CCI Scores		SAC
37.	Screened	HO_02	Listing of CCI Questionnaire Results at Day 8		SAC
38.	Screened	HO_03	Listing of CCI from Daily Diary Cards		SAC

11.9.11. Mock Displays

Protocol: 208832 Page 1 of 1
Population: Safety

Table DISP_T1
Summary of Subject Disposition at Each Study Phase

Study Phase		Total (N=200)
Oral Lead-in Phase	ENTERED	xx (xx.x%)
	COMPLETED	xx (xx.x%)
	WITHDRAWN	xx (xx.x%)
	COVID-19 RELATED[1]	xx (xx.x%)
Injection Phase	ENTERED	xx (xx.x%)
	COMPLETED	xx (xx.x%)
	WITHDRAWN	xx (xx.x%)
	COVID-19 RELATED[1]	xx (xx.x%)
Follow-up Phase	ENTERED	xx (xx.x%)
	COMPLETED	xx (xx.x%)
	WITHDRAWN	xx (xx.x%)
	COVID-19 RELATED[1]	xx (xx.x%)

[1] Covid-19 Related Disposition as collected from the Study Impact record

Protocol: 208832
Page 1 of 1
Population: Safety

Table DISP_T2
Summary of Reasons for Withdrawal at Each Study Phase

Primary Reason	Oral CAB 30mg + Oral RPV 25mg (N=100)	IM CAB 600mg + IM RPV 900mg – Injection Phase (N=100)	IM CAB 600mg + IM RPV 900mg – Follow-up Phase (N=100)	Overall (N=100)
ADVERSE EVENT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 RELATED[1]	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
PROTOCOL DEVIATION	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 RELATED[1]	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
SUBJECT REACHED PROTOCOL-DEFINED STOPPING CRITERIA	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
STUDY TERMINATED BY SPONSOR	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
LOST TO FOLLOW-UP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
INVESTIGATOR SITE CLOSED	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PHYSICIAN DECISION	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
WITHDRAWAL BY SUBJECT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 RELATED[1]	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)

[1] Covid-19 Related Disposition as collected from the Study Impact record

Protocol: 208832

Population: Pharmacokinetic Parameter

PK_01

Summary of Derived Cabotegravir Pharmacokinetic Parameters by Phase

Parameter	Summary Statistics	Oral CAB 30mg (N=xx)	IM CAB 600 mg (N=xx)
AUC_{0-t} (h*μg/mL)	n	xx	xx
	Mean (SD)	Xxx.x (xx.xx)	Xxx.x (xx.xx)
	95% CI	(xxx.xx,xxx.xx)	(xxx.xx,xxx.xx)
	%CV	xx.x	xx.x
	Median	xxx.xx	xxx.xx
	Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	Geometric mean	xxx.xx	xxx.xx
	95% CI	(xxx.xxx,xxx.xxx)	(xxx.xxx,xxx.xxx)
	SD (log)	xxx.xxx	xxx.xxx
	Geometric %CV	xxx.x	xxx.x
$AUC_{0-\infty}$ (h*μg/mL)	n	xx	xx
	Mean (SD)	Xxx.x (xx.xx)	Xxx.x (xx.xx)
	95% CI	(xxx.xx,xxx.xx)	(xxx.xx,xxx.xx)
	%CV	xx.x	xx.x
	Median	xxx.xx	xxx.xx
	Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	Geometric mean	xxx.xx	xxx.xx
	95% CI	(xxx.xxx,xxx.xxx)	(xxx.xxx,xxx.xxx)
	SD (log)	xxx.xxx	xxx.xxx

Geometric %CV	xxx.x	xxx.x

/Directory/program.sas 01JAN2002 12:01

Programming notes:

1) Repeat table for RPV (Oral RPV 25mg, IM RPV 900mg; ng/mL, ng*h/mL)
2) Repeat for all of the following PK parameters as available: C_{max}, t_{max}, $t_{1/2}$, K_A LA, λz, C24, Cτ
3) For t_{max}, only the n, median, minimum, and maximum should be provided.
4) Report the means & median +1 decimal past the maximum length of results within parameter. Report the SD and 95% CI values +2 decimals past the maximum length of results within parameter. %CV statistics should be reported to 1 decimal.

Protocol: 208832
Population: Screened

HO 01

Listing of CCI [redacted] Scores

Treatment	Site Id./ Unique Subject Id.	Treatment/ Injection Site Side	Visit	Date	CCI
Treatment A	PPD [redacted]	CAB/Left	Day 1	YYYY-MM-DDTHH:MM	[redacted]
			Day 2	YYYY-MM-DDTHH:MM	
			Day 4	YYYY-MM-DDTHH:MM	
			Day 5	YYYY-MM-DDTHH:MM	
			Day 8	YYYY-MM-DDTHH:MM	
		RPV/Right	Day 1	YYYY-MM-DDTHH:MM	

USER ID:/PROGRAM PATH/PROGRAM DATE TIME

Protocol: 208832
Population: Screened

HO 02

Listing of [redacted] Results at Day 8

Treatment: Treatment A

Site Id./ Unique Subject Id.	Date/Time of Assessment	Treatment/ Injection Site Side/	Domain	Question	Result
PPD	YYYY-MM-DD/ HH:MM	CAB/Left	CCI	[redacted]	
			...		
	YYYY-MM-DD/ HH:MM	RPV/Right			

CCI [redacted]

USER ID:/PROGRAM PATH/PROGRAM DATE TIME

Protocol: 208832
Population: Screened

HO_03
Listing of Injection Area Symptoms from Daily Diary Cards

Treatment	Site Id./ Unique Subject Id.	Treatment/ Injection Site Side	Date of Assessment/ Study Day	Symptoms? (Y/N)	Pain (0-3)	Itching (0-3)	Other Symptoms [1]	Home Treatment [2]
Treatment A	PPD	CAB/ Left	YYYY-MM-DD/ 1	Y	2	1	BU, SF	AP, Top
			YYYY-MM-DD/ 2	Y	0	1		Top
			...					
		RPV/ Right	YYYY-MM-DD/ 1	N				
			...					

[1] NO=None, BR=Bruising, BU=Bump, D=Discoloration, R=Redness, SF=Skin firmness, SW=Swelling, W=Warm to touch.
[2] NO=None, AP=Acetaminophen/paracetamol (Tylenol), D=Diphenhydramine (Benadryl), Top=Topical anti-itch cream or ointment such as hydrocortisone/diphenhydramine, etc., W=Warm compress (heating pad), C=Cold compress (cold pack or ice pack).

USER ID:/PROGRAM PATH/PROGRAM DATE TIME

11.10. Appendix 10: AESI Identification

SMQ and PT codes based on MedDRA dictionary version 23.0.

11.10.1. Hepatotoxicity

SMQ: Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions SMQ Code: 20000013 Category: A Scope: Narrow	
Preferred Term	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
Cardiohepatic syndrome	10082480
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
Gastrooesophageal variceal haemorrhage prophylaxis	10066597
Hepatectomy	10061997
Hepatic atrophy	10019637
Hepatic calcification	10065274
Hepatic cirrhosis	10019641
Hepatic encephalopathy	10019660
Hepatic encephalopathy prophylaxis	10066599
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
Immune-mediated cholangitis	10083406
Immune-mediated hepatic disorder	10083521
Intestinal varices	10071502
Intestinal varices haemorrhage	10078058
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
Nonalcoholic fatty liver disease	10082249
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
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
Sugiura procedure	10083010
Varices oesophageal	10056091
Varicose veins of abdominal wall	10072284
White nipple sign	10078438
SMQ: Hepatitis, non-infectious SMQ Code: 20000010 Category: A Scope: Narrow	
Preferred Term	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

11.10.2. Seizures

SMQ: 'Convulsions' SMQ Code: 20000079 Category: A Scope: Narrow	
Preferred Term	PT Code
1p36 deletion syndrome	10082398
2-Hydroxyglutaric aciduria	10078971
Acquired epileptic aphasia	10052075
Acute encephalitis with refractory, repetitive partial seizures	10076948
Alcoholic seizure	10056347
Alpers disease	10083857
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
CEC syndrome	10083749
CDKL5 deficiency disorder	10083005
Change in seizure presentation	10075606
Clonic convulsion	10053398
Congenital bilateral perisylvian syndrome	10082716

Convulsion in childhood	10052391
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
Gelastic seizure	10082918
Generalised onset non-motor seizure	10083376
Generalised tonic-clonic seizure	10018100
Glucose transporter type 1 deficiency syndrome	10078727
GM2 gangliosidosis	10083933
Grey matter heterotopia	10082084
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
Neonatal epileptic seizure	10082068
Neonatal seizure	10082067
Partial seizures	10061334
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
Additional selected preferred terms from HLT “Disturbances in consciousness NEC” (Code: 10013509) under SOC “Nervous systems disorders” and HLT “Confusion and disorientation” (Code: 10010301) under SOC “Psychiatric disorders”.	
Preferred Term	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

11.10.3. Torsade de pointes/QT prolongation

Notes: Medical concept of QT prolongation and complications. Only narrow terms from SMQ 'Torsade de pointes/QT prolongation' selected plus one additional PT under HLT ‘ECG investigations'.

SMQ: Torsade de pointes/QT prolongation SMQ Code: 20000001 Category: A Scope: Narrow	
Preferred Term	PT Code
Electrocardiogram QT interval abnormal	10063748
Electrocardiogram QT prolonged	10014387
Long QT syndrome	10024803
Long QT syndrome congenital	10057926
Torsade de pointes	10044066
Ventricular tachycardia	10047302
Additional preferred terms selected from HLT ' ECG investigations' (Code: 10053104) under SOC 'Investigations'.	
Preferred Term	PT Code
Electrocardiogram repolarisation abnormality	10052464

11.10.4. COVID-19 Adverse Events

COVID-19 adverse events are identified based on MedDRA coded values and/or AE referenced in the COVID-19 Coronavirus Infection assessment. The Lowest Level Terms (LLTs) and codes, Preferred Terms (PTs), High Level Terms (HLTs), High Level Group Terms (HLGTs), and System Organ Classes (SOCs), below are from MedDRA 23.0. 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.

SOC: Infections and infestations

LLT code	LLT	PT	HLT	HLGT
10084459	Asymptomatic COVID-19	Asymptomatic COVID-19	Coronavirus infections	Viral infectious disorders

LLT code	LLT	PT	HLT	HLGT
10084467	Asymptomatic SARS-CoV-2 infection	Asymptomatic COVID-19	Coronavirus infections	Viral infectious disorders
10053983	Corona virus infection	Coronavirus infection	Coronavirus infections	Viral infectious disorders
10051905	Coronavirus infection	Coronavirus infection	Coronavirus infections	Viral infectious disorders
10084382	Coronavirus disease 2019	COVID-19	Coronavirus infections	Viral infectious disorders
10070255	Coronavirus test positive	Coronavirus test positive	Virus identification and serology	Microbiology and serology investigations

10084460	COVID-19 treatment	COVID-19 treatment	Antiinfective therapies	Therapeutic procedures and supportive care NEC
10084639	SARS-CoV-2 sepsis	SARS-CoV-2 sepsis	Coronavirus infections	Viral infectious disorders
10084271	SARS-CoV-2 test positive	SARS-CoV-2 test positive	Virus identification and serology	Microbiology and serology investigations
10084640	SARS CoV-2 viraemia	SARS CoV-2 viraemia	Coronavirus infections	Viral infectious disorders
10084268	COVID-19	COVID-19	Coronavirus infections	Viral infectious disorders
10084401	COVID-19 respiratory infection	COVID-19	Coronavirus infections	Viral infectious disorders
10084270	SARS-CoV-2 acute respiratory disease	COVID-19	Coronavirus infections	Viral infectious disorders
10084272	SARS-CoV-2 infection	COVID-19	Coronavirus infections	Viral infectious disorders
10084381	Coronavirus pneumonia	COVID-19 pneumonia	Coronavirus infections	Viral infectious disorders
10084380	COVID-19 pneumonia	COVID-19 pneumonia	Coronavirus infections	Viral infectious disorders
10084383	Novel COVID-19-infected pneumonia	COVID-19 pneumonia	Coronavirus infections	Viral infectious disorders
10084451	Suspected COVID-19	Suspected COVID-19	Coronavirus infections	Viral infectious disorders
10084452	Suspected SARS-CoV-2 infection	Suspected COVID-19	Coronavirus infections	Viral infectious disorders
10084461	SARS-CoV-2 carrier	SARS-CoV-2 carrier	Infectious disorders carrier	Ancillary infectious topics