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

Title	:	Phase I, single-center, open label, fixed-sequence cross-over study to evaluate the effect of rifabutin on the pharmacokinetics of oral cabotegravir in healthy subjects
Compound Number	:	GSK1265744
Effective Date	:	08-SEP-2017

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Pharmacology Study Report for Protocol 205712
- This RAP is intended to describe the safety, pharmacokinetics (PK), 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.

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for Protocol 205712:

Revision Chronology:		
GSK Document No.: 2016N269788_00	23-FEB-2017	Original
GSK Document No.: 2016N269788_01	13-APR-2017	The purpose of this protocol amendment is to update Appendix 12.5.1." Modified List of Highly Effective Methods for Avoiding Pregnancy in Females of Reproductive Potential(FRP)". The updates include clarifying true abstinence for this study and the deletion of double barrier method: condom and occlusive cap (diaphragm or cervical/vault caps) plus spermicidal agent foam/gel/film/cream/suppository) as a highly effective method for avoiding pregnancy in females of reproductive potential (FRP)
GSK Document No.: 2016N269788_02	29-JUN-2017	Clarify the required days for fasting (Day 14 and Day 28). Remove Appendix 12.4.3- Definition of Cardiovascular Events. The collection of Cardiovascular Events is not applicable to the 205712 study.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the protocol amendment 2 (Dated: 29-Jun-2017).

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

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To compare steady state CAB exposure following 30 mg oral dose once daily with and without RBT 300 mg once daily.	• Plasma CAB AUC(0-τ), Cmax
Secondary Objectives	**Secondary Endpoints**
• To describe the pharmacokinetic (PK) of CAB 30 mg oral dose once daily administered alone and co-administered with RBT.	• Plasma CAB Cτ, tmax, t1/2 and CL/F
• To assess the safety and tolerability of CAB 30 mg oral dose administered alone and in combination with RBT 300 mg once daily.	• Safety and tolerability parameters, including adverse events, concurrent medication, clinical laboratory screens, electrocardiogram (ECG), and vital signs assessments.
$AUC_{(0-t)}$ = area under the plasma concentration time curve from time zero to the last quantifiable time point C_{max} = maximum observed concentration Ct = last quantifiable concentration t_{max} = time of maximum observed concentration $t_{1/2}$ = the elimination half-lifeCL/F = apparent oral clearance	

2.3. Study Design

Overview of Study Design and Key Features

Table 1 Study Design

Subjects	Screening Period	Period 1 Days 1 – 14	Period 2 Days 15 - 28	Follow-up
N=15	Within 30 Days of Day 1	Treatment A	Treatment B	~10-14 days after last dose of CAB

- Treatment A = CAB 30 mg once daily x 14 days
- Treatment B = RBT 300 mg once daily + CAB 30 mg once daily x 14 days

Design Features	This study is a phase I, single-center, open label, fixed-sequence, 2-period crossover study in healthy adults.
Dosing	Subjects will undergo a screening visit within 30 days of the first dose of study drug, followed by two treatment periods and a follow-up period. • Approximately 15 healthy adult subjects will be enrolled to ensure that 12 subjects will complete dosing and critical assessments. • **Period 1**: Eligible participants will be admitted to the unit on Day -1. Subjects will be dosed for Days 1, 13 and 14 under the fasting conditions in the unit and subjects will be dispensed a bottle of CAB to be taken at home on Days 2-12 and discharged from the unit. Subjects will be provided with a subject diary to document daily recordings of dosing occurring outside of the unit. There will be no washout between Period 1 and Period 2. • **Period 2:** On Day 15 following the completion of the required Day 14 safety assessments and PK collection, subjects will proceed to Period 2, where site staff will administer a single dose of RBT 300 mg and a single dose of CAB 30 mg after an overnight fast of at least 6 hours in the unit. Subjects will be discharged and dispensed a bottle of RBT and a bottle of CAB to be taken at home on Days 16-20 and 22-25. Subjects will be provided with a subject diary to document daily recordings of home dosing. In the morning of Days 21, subjects will bring their bottle of RBT and bottle of CAB for observed dosing in the unit and safety assessments as an outpatient visit. On Days 26 and 27, subjects will return to the unit for a pre-dose PK collection and observed dosing as an outpatient visit and then be discharged home. In the morning of Day 28 following an overnight fast of at least 6 hours, subjects will receive a single dose of RBT and a single dose of CAB in the unit with serial CAB PK samples collected pre-dose and through 24 hours after dosing up to Day 29. • Subjects will be discharged from the unit on Day 29 after the final assessment is completed. Subjects will complete a follow-up visit ~ 10-14 days after the last 30 mg oral dose of CAB.

Overview of Study Design and Key Features	
Treatment Assignment	Subjects will receive following treatments in a fixed sequence of A/B: • Treatment A = CAB 30 mg once daily x 14 days • Treatment B = RBT 300 mg once daily + CAB 30 mg once daily x 14 days
Interim Analysis	• No interim analysis will be performed.

2.4. Statistical Hypotheses

No formal hypothesis will be tested. This study is designed to estimate the drug-interaction effect of RBT on CAB PK parameters. An estimation approach will be used to evaluate the effect of RBT on CAB PK. Point estimates and corresponding 90% confidence intervals (CIs) will be constructed for the comparisons of interest (test:reference).

3. PLANNED ANALYSIS

3.1. Interim Analyses

- No interim analysis will be performed.

3.2. Final Analyses

Final analyses will be performed after the completion of the study, following sequential steps and final database authorization:

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

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screening Population	All subjects who sign the consent form will be included in this population.	• Screening population listing and summary
Safety Population	All subjects who enrol in the study and receive at least one dose of study drug will be included in the Safety Population.	• Study Population • Safety
PK Concentration Population	The CAB PK Concentration Population will include all subjects who undergo plasma PK sampling and have evaluable PK assay results.	• PK concentration listing, and individual concentration plot
PK Parameter Population	The PK Parameter Population will include all subjects who have evaluable PK parameters. Data from subjects who vomit within 4 hours of study drug administration will not be considered as evaluable.	• PK parameter listing, and plotting
PK Summary Population	The CAB PK Summary Population for this study will include subjects who have CAB PK parameter estimates from both serial PK sampling time periods 1 and 2. These populations will be used for the concentration and PK parameters summary figures and tables and for the statistical analysis of PK parameter data	• PK concentrations and summary table and summary figures • PK Parameter Summary table • Statistical analysis of parameter data

NOTES :

- Please refer to Appendix 11 which details the population to be used for each display being generated.

4.1. Protocol Deviations

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

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

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

Table 2 provides an overview of appendices within the RAP for outlining general considerations for data analyses and data handling conventions.

Table 2 Overview of Appendices

Section	Component
Section 10.1	Appendix 1: Protocol Deviation Management
Section 10.2	Appendix 2: Data Management
Section 10.3	Appendix 3: Time & Events
Section 10.4	Appendix 4: Treatment States and Phases
Section 10.5	Appendix 5: Data Display Standards & Handling Conventions
Section 10.6	Appendix 6: Derived and Transformed Data
Section 10.7	Appendix 7: Premature Withdrawals & Handling of Missing Data
Section 10.8	Appendix 8: Values of Potential Clinical Importance
Section 10.9	Appendix 9: Model Checking and Diagnostics for Statistical Analyses.
Section 10.10	Appendix 10: Abbreviations and Trade Marks
Section 10.11	Appendix 11: List of Data Displays
Section 10.12	Appendix 12: Example Mock Shells for Data Displays

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Analyses

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

Table 3 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 11: List of Data Displays.

Table 3 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Figure	Table	Listing
Study Population			
Analysis Population Summary		Y	
Subject Disposition			
Subject Disposition		Y	Y

Display Type	Data Displays Generated		
	Figure	Table	Listing
Protocol Deviations		Y	Y
Inclusion and Exclusion Criteria Deviations			Y
Demography			
Demographics Characteristics		Y	Y
Race & Racial Combinations		Y	Y
Age Group Breakdown for Trial		Y	
Others			
Concomitant Medication		Y[1]	Y
Genetic sample collection			Y
Random codes			Y
Treatment non-compliance			Y
Screening information		Y[2]	Y[3]

NOTES:

- Y = Yes display generated.

1. Conditional display, if data contains more than 10 records.
2. Screening population.
3. All screen failures

7. PRIMARY STATISTICAL ANALYSES

7.1. Pharmacokinetic Analyses

The reconciliation of the PK Case Report Form (CRF) and SMS2000 data will be performed by Data Management, QSci at GlaxoSmithKline.

The merge of PK concentration data, randomization and CRF data will be performed. The analysis PK concentration dataset and WinNonLin files will be created by statistics and programming, under the direct auspices of statistics and programming, Quantitative Sciences (QSci), GlaxoSmithKline.

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

Statistical Analysis of pharmacokinetic parameters will be performed by statistics and programming under the direct auspices of statistics and programming, QSci, GlaxoSmithKline.

7.1.1. Overview of Planned Pharmacokinetic Analyses

The pharmacokinetic (PK) analyses will be based on the PK Concentration, PK Parameter, or PK Summary populations where it is specified.

Table 4 provides an overview of the planned analyses, with full details being presented in Appendix 11: List of Data Displays.

Table 4 Overview of Planned Pharmacokinetic Analyses

Endpoints	Untransformed				Log_e-Transformed			
	Summary		Individual		Summary		Individual	
	F	T	F	L	F	T	F	L
Plasma Drug Concentrations	Y [1] [2]	Y	Y [1]	Y	Y [1] [2]		Y [1]	
Derived PK Parameters		Y	Y[3]	Y		Y	Y[3]	
Statistical Analysis PK Parameters					Y[4]	Y		Y[5]

NOTES :

- T = Table, F = Figures, L = Listings, Y = Yes display generated.
- Summary = Represents TF related to any summaries (descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- Tmax is not log transformed.

1. Linear and Semi-Log plots will be created on the same display.
2. Mean (+SD) and Median plots will be generated.
3. Comparative Plot of Individual CAB Plasma PK Parameter vs treatments on linear and semi-log scale
4. Geometric Mean Treatment Ratio and 90% CI of CAB Plasma PK Parameters will be generated.
5. Supportive SAS Output from Statistical Analysis of Log_e-transformed CAB Plasma PK Parameters

7.1.2. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Process & Standards).

7.1.3. Pharmacokinetic Parameters

PK analyses will be the responsibility of the CPMS department within GSK or their designee. Plasma CAB concentration-time data will be analyzed by non-compartmental methods according to current working practices and using Phoenix WinNonlin 6.3 or higher. Calculations will be based on the actual sampling times recorded during the study and based on nominal sampling times. From the plasma concentration-time data, the following PK parameters will be determined, as data permit: Cmax, Tmax, Cτ, t1/2, AUC(0-τ) and CL/F.

Statistics and Programming group will calculate the individual ratios for Cmax, Cτ and AUC(0-τ).

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Process & Standards).

Non-compartmental analysis will be performed in accordance with GSK PK Guidance document GUI_51487.

Refer Appendix 7 Section 10.7.2.2 for handling of PK Concentration data.

Table 5 Derived Pharmacokinetic Parameters

Parameter	Parameter Description
AUC(0-τ)	Area under the plasma concentration-time curve at the end of the dosing interval will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
Cmax	Maximum observed concentration, determined directly from the concentration-time data.
Cτ	Plasma concentration at the end of the dosing interval
Tmax	Time to reach Cmax, determined directly from the concentration-time data.
t½	Apparent terminal half-life will be calculated as: t½ = ln2 / Lambda_z (NOTE: Lambda_z is the terminal phase rate constant).
CL/F	The apparent oral clearance (CL/F) will be calculated as CL/F = Dose/AUC(0-τ)

PK parameters that have mass in the units should be reported in μg/mL and h•μg/mL for CAB. CL/F should be reported in units of L/h.

7.2. Statistical Analysis of Pharmacokinetic Parameters

All PK data will be stored in the Archives, GlaxoSmithKline R& D. Statistical analyses of the PK parameter data will be the responsibility of Clinical Statistics, GlaxoSmithKline or their designee.

For each of the parameters Cmax, Cτ , AUC(0-τ), t1/2 and CL/F, if data permit, the following summary statistics will be calculated and tabulated by treatment :

- **Untransformed Data :** N, n, arithmetic mean, SD, median, minimum, maximum and %CV.
- **Log_e-transformed Data:** Geometric mean, 95% CI for the geometric mean, SD of log_e-transformed data and %CVb

For Tmax , the summary statistics specified for untransformed data above will be generated.

Primary and Secondary Comparisons of Interest

	CAB PK Parameter	Test	Reference	Assessment
Primary	Cmax and AUC(0-τ)	Treatment B: RBT+CAB	Treatment A: CAB	Interaction
Secondary	Cτ, t1/2 and CL/F	Treatment B: RBT+CAB	Treatment A: CAB	

The PK parameters for CAB (except T_{max}) will be log_e-transformed and separately analyzed using a mixed effects model. Analysis of variance (ANOVA), considering treatment as fixed effect and subject will be treated as a random effect in the model, will

be performed using SAS Mixed Linear Models procedure to evaluate the effect of RBT on CAB PK parameters: AUC(0-τ) and Cmax. Similar model will be applied for secondary endpoints: Cτ, t1/2 and CL/F. Point estimates and their associated 90% CIs will be constructed for the differences in PK parameter values between RBT+CAB and CAB alone for the treatment comparisons. The point estimates and their associated 90% CIs will then be back-transformed to provide point estimates and 90% CIs for the ratios of PK parameters between test and reference treatments.

Estimates of within-subject variability for Cmax, Cτ , t1/2, AUC(0-τ) and CL/F will be provided, where CVw(%) = SQRT(exp(MSE) – 1)×100 and MSE is the residual mean squared error from the model. CVw represents a pooled measure of within-subject variability across the treatments CAB and RBT+CAB.

Pre-dose concentrations collected between Days 13-14 and Days 26-28 will be listed with PK concentration profiles and summarized by Day/Time. To assess for achievement of steady-state of CAB when CAB is given with RBT, Analysis of variance (ANOVA), considering DAY as fixed effect and subject as a random effect in the model, will be performed using SAS Mixed Linear Model on the pre-dose concentration between Days. The estimated slope and 90% CI will be presented for models included 2 days (Days 13-14, 27-28) or 3 days (Days 26-28) pre-dose concentrations.

Comparative Plot of Individual subject CAB Plasma PK Parameter Versus Treatment will be generated.

Individual and box plots of Pre-dose concentration of Day 13-14 and Days 26-28 will be generated.

Plots will also be provided showing the adjusted geometric mean ratio of test to reference treatment for Cmax, Cτ, AUC(0-τ), t1/2 and CL/F with 90% CIs.

The SAS output from the statistical models will be included in a listing of supportive SAS output.

8. SECONDARY STATISTICAL ANALYSES

8.1. Safety Analyses

8.1.1. Overview of Planned Analyses

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

Table 6 provides an overview of the planned analyses, with full details of data displays being presented in Appendix 11: List of Data Displays.

Table 6 Overview of Planned Safety Analyses

Endpoint	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Exposure								
Exposure	Y			Y				
Adverse Events								
All AE's	Y			Y				
Serious AE's				Y				
Drug Related AEs	Y			Y[1]				
Withdrawal AE's	Y			Y				
Relationship Between System Organ Class and Verbatim Text				Y				
Liver Event				Y				
Laboratory Values								
Clinical Chemistry	Y			Y[2]				
Hematology	Y			Y[2]				
Clinical Lab Reference Ranges				Y				
Treatment Emergent Toxicity Grade	Y							
Urinalysis	Y			Y				
ECG's								
ECG Findings	Y			Y				
ECG Values	Y			Y[2]	Y			
Category of QTc Data	Y				Y			
ECG Values Outside the PCI Range				Y				
Vital Signs								
Vitals Values	Y			Y[2]	Y			
Vital Signs Measurements Outside the PCI Range				Y				

NOTES :

- T = Table, F = Figures, L = Listings, Y = Yes display generated.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

1: Part of all AEs listing

2: Listing will include toxicity grade or flag for H/L if out of normal range

9. REFERENCES

GlaxoSmithKline Document Number 2016N269788_00: Phase I, single-center, open label, fixed-sequence cross-over study to evaluate the effect of rifabutin on the pharmacokinetics of oral cabotegravir in healthy subjects. Effective Date: 23-FEB-2017

GlaxoSmithKline Document Number 2016N269788_01: Phase I, single-center, open label, fixed-sequence cross-over study to evaluate the effect of rifabutin on the pharmacokinetics of oral cabotegravir in healthy subjects Effective Date: 13-APR-2107

GlaxoSmithKline Document Number 2016N269788_02: Phase I, single-center, open label, fixed-sequence cross-over study to evaluate the effect of rifabutin on the pharmacokinetics of oral cabotegravir in healthy subjects Effective Date: 29-Jun-2017

10. APPENDICES

Section	Appendix
RAP Section 4: Analysis Populations	
Section 10.1	Appendix 1: Protocol Deviation Management
RAP Section 5 : General Considerations for Data Analyses & Data Handling Conventions	
Section 10.2	Appendix 2: Data Management
Section 10.3	Appendix 3: Time and Events
Section 10.4	Appendix 4: Treatment States & Phases
Section 10.5	Appendix 5: Data Display Standards & Handling Conventions • Study Treatment & Sub-group Display Descriptors • Baseline Definitions & Derivations • Reporting Process & Standards
Section 10.6	Appendix 6: Derived and Transformed Data • General • Study Population • Safety • Pharmacokinetic
Section 10.7	Appendix 7: Premature Withdrawals & Handling of Missing Data • General • Study Population & Safety
Section 10.8	Appendix 8: Values of Potential Clinical Importance • Laboratory Values • ECG • Vital Signs
Section 10.9	Appendix 9: Model Specifications for Statistical Analyses
Other RAP Appendices	
Section 10.10	Appendix 10: Abbreviations & Trade Marks
Section 10.11	Appendix 11: List of Data Displays
Section 10.12	Appendix 12: Example Mock Shells for Data Displays

10.1. Appendix 1: Protocol Deviation Management

10.1.1. Exclusions from PK Parameter Summary Population

All protocol deviations will be reviewed, and only the important deviations will be listed and summarized. Some subjects may be excluded from analysis due to protocol deviations. A subject meeting any of the following criteria will be excluded from the PK Parameter Summary Population:

Number	Exclusion Description
01	Failure of any inclusion/exclusion criteria, but subject is still enrolled
02	A subject with emesis occurring within 4 hours of the dose on Day 14 or Day 28
03	A subject who does not have evaluable PK parameters from both periods
04	A subject who has not dosed correctly on the days for PK collections

10.2. Appendix 2: Data Management

10.2.1. Data Format and Process

Data Type	Source	Format of Data	Planned Date of Final File	Responsibility
Safety	PIMS>SI data	SI>STDM	DBF	Accenture
PK Concentration	SMS2000 data file	dat file	DBF	BIB/BESM
PK Concentration (ADPC), WNL File	PK concentration data (SDTM PC), exposure (EX) and demography (DM) datasets[2]	ADaM, CSV file	DBF + 5 Days[1]	QSci
PK Parameters	WNL file	CSV file	PK Concentration, WNL file + 10 Days	CPMS

1. Provided SDTM PC, EX and DM are in time and clean
2. PK concentration data is released via SMS2000 by Bioanalysis, Immunogenicity and Biomarkers (BIB)/Bioanalytical External Study Monitors (BESM) and the SDTM PC contains date/times and PK sample ID

10.3. Appendix 3: Time & Events

10.3.1. Protocol Defined Time & Events

Procedure	Screen[1]	Day -1	Treatment Period 1 Day													Treatment Period 2 Day															Early Withdrawal / Follow-up ~10-14 days
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21[2]	22	23	24	25	26[2]	27	28	29	
Informed consent	X																															
Inclusion and exclusion criteria	X	X																														
Demography	X																															
Full physical exam[3]	X																															
Brief physical exam[3]		X														X							X							X	X[4]
Medical/medication/drug/alcohol history	X	X														X							X									
Pregnancy test [5]	X	X														X													X			X
FSH and estradiol (if needed)	X																															
TB, HIV, Hep B, Hep C screen	X																															
Drug/Alcohol screen	X	X													X														X			

Procedure	Screen[1]	Day -1	Treatment Period 1 Day													Treatment Period 2 Day															Early Withdrawal / Follow-up ~10-14 days
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21[2]	22	23	24	25	26[2]	27	28	29	
Safety Laboratory assessments	X	X													X								X						X			X
12-lead ECG[6]	X		X													X														X		X
Vital signs (Including Temperature)[6]	X		X													X							X							X		X
Administer CAB 30 mg once daily[7]			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Administer RBT 300 mg once daily[7]																	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Dispense CAB[8]			X																													
Dispense CAB[9]and RBT[10]																	X															
Pharmacokinetic Sampling[11]															X	X-----X												X	X	X----- X		
Admit to Unit		X													X														X			
Discharge from Unit			X														X														X	
Outpatient Visit	X																						X					X				X

Procedure	Screen[1]	Day -1	Treatment Period 1 Day													Treatment Period 2 Day														Early Withdrawal / Follow-up ~10-14 days
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21[2]	22	23	24	25	26[2]	27	28	29	
Drug accountability															X								X					X	X			
Genetic sample[12]			←==========→																													
SAE Review	←==========→																															
AE Review			←==========→																													
Concomitant medication review			←==========→																													

1. Screening must be performed within 30 days prior to receiving the dose of CAB on Day 1.
2. Day 21 and Day 26 is an outpatient visit.
3. An ocular assessment will be performed only for subjects who experience eye symptoms.
4. A brief symptom directed physical exam will be completed as needed.
5. A serum pregnancy test will be performed at the screening visit and a urine pregnancy test at all other time points specified.
6. Duplicate ECG, BP, and HR assessments will be conducted pre-dose on Day 1. Single measurements will be collected at all other time points.
7. Study medication will be administered with 240 mL of water within the unit on Days 1, 13, 14, 15, 21, 26, 27, and 28. Dosing on non-PK days may be with or without food, but dosing on serial PK days (Day 14 in Period 1 and Day 28 in Period 2) must be after an overnight fast of at least 6 hours, and no food will be allowed for 4 hours after dosing on these serial PK days.
8. Dispense the bottle of CAB tablets to the subject on Day 1 to receive CAB dosing at home on Days 2 to 12 in Period 1
9. Dispense the bottle of CAB tablets to the subject on Day 15 to receive CAB dosing at home on Days 16 to 20 and Days 22 to 25 in Period 2; dosing on Day 21, 26, 27, and 28 is in the unit.
10. Dispense the bottle of RBT capsules to the subject on Day 15 to receive RBT dosing at home on Days 16 to 20 and Days 22 to 25 in Period 2; dosing on Day 21, 26, 27, and 28 is in the unit.
11. Plasma PK samples (2 mL of blood per sample) will be collected to measure CAB at the following time points: Period 1: predose (within 15 minutes prior to dose) on Day 13; and pre-dose (within 15 minutes prior to dose), 1, 2, 3, 4, 8, 12, and 24 hours after CAB dosing on Day 14. Period 2: pre-dose (within 15 minutes prior to dose) on Days 26 and 27 and pre-dose (within 15 minutes prior to dose) on Day 28 and, 1, 2, 3, 4, 8, 12, and 24 hours after CAB +RBT dosing on Day 28.
12. It is recommended that the Pharmacogenetic sample be collected on Day 1, but it may be collected at any time following administration of investigational product.

10.4. Appendix 4: Treatment States and Phases

10.4.1. Treatment State and Study Phases

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

Treatment State	Study Phase
Pre-Treatment	Screening assessments collected prior to the Day 1 visit
On-Treatment	Period 1 and Period 2
Follow-up	Follow-up Visit

10.4.1.1. Treatment States for AE, SAE and Concomitant Medications Data

Treatment State	Definition
Screening	AE(SAE or conmed) Start Date/Time < Study Treatment Start Date/Time. Based on the protocol, these AEs and concomitant medications prior to dosing will not be collected in database, and only record in the source document, but SAE will be captured on the dataset
Treatment A	If AE (SAE or conmed) onset date/time is on or after Period 1 treatment start date/time & before Period 2 treatment date/time Study Period 1 Treatment Start Date/Time ≤ AE Start Date/Time < Study Period 2 Treatment Date/Time]
Treatment B	If AE (SAE or conmed) onset date/time is on or after Period 2 treatment start date/time & before Study Conclusion date/time Study Period 2 Treatment Start Date/Time ≤ AE Start Date/Time < Study follow-up visit Date/Time]
Follow-up	All unsolved AEs (SAE or conmed) during the follow-up will be associated with the treatment from Period 2, and no AEs (SAE or conmed) will be report under the follow-up
Onset Time Since First Dose (Days)	If Treatment Start Date/Time > AE Onset Date/Time = AE Onset Date - Treatment Start Date If Treatment Start Date/Time ≤ AE Onset Date/Time = AE Onset Date - Treatment Start Date +1 Missing otherwise
Duration (Days)	AE Resolution Date – AE Onset Date + 1
Drug-related	If relationship is marked 'YES' on eCRF

NOTES:

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

10.4.1.2. Reporting Other Safety Data

All of other safety measurements will be associated and summarized for each visit based on the CRF as the following:

Visit	Time Slices Definition
Screening	Screen
Period 1	Day -1, Period 1 Days 1-Day 14
Period 2	Period 2, Days 15-28
Follow-up	Follow-up

10.5. Appendix 5: Data Display Standards & Handling Conventions

10.5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions		
RandAll NG		Data Displays for Reporting
Code	Description and Footnotes for the Displays	Description
A	CAB 30 mg once daily x 14 days	CAB 30mg
B	RBT 300 mg once daily + CAB 30 mg once daily x 14 days	RBT 300mg + CAB 30mg

10.5.2. Baseline Definition & Derivations

10.5.2.1. Baseline Definitions

For all endpoints (except as noted in the table) the baseline value will be the latest pre-dose assessment.

Table 7 Baseline Definitions

Parameter	Study Assessments Considered as Baseline			Baseline Used in Data Display
	Screening	Day -1	Day 1 (Pre-Dose)	
Safety				
Labs	X	X		Day -1
ECG			X	Day 1 (Pre-Dose)
Vital Signs (blood pressure, and pulse rate)	X		X	Day 1 (Pre-Dose)

10.5.2.2. Derivations and Handling of Missing Baseline Data

Definition	Reporting Details
Change from Baseline	= Post-Dose Visit Value – Baseline

NOTES:

- Unless otherwise specified, the baseline definitions specified in Section 10.5.2.1 Baseline Definitions will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.
- The baseline definition will be footnoted on all change from baseline displays.

10.5.3. Reporting Process & Standards

Reporting Process	
Software	
• The currently supported versions of SAS and S-Plus software will be used.	
Reporting Area	
HARP Server	: US1SALX00259-HARP PROD-US
HARP Area	: \ARPROD\GSK1265744\mid205712\Final
QC Spreadsheet	: \ARWORK\GSK1265744\mid205712\Final\Documents
Analysis Datasets	
• Analysis datasets will be created according to Clinical Data Interchange Standards Consortium (CDISC) standards (SDTM IG Version 3.1.3 or higher vision & Analysis Data Model (ADaM) Implementation Guide (ADaM IG) Version 1.1 or higher dataset standards)	
Generation of Rich Text Format (RTF) Files	
• RTF files will be generated for Safety summary displays.	

Reporting Standard
General
• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated: o 4.03 to 4.23: General Principles o 5.01 to 5.08: Principles Related to Data Listings o 6.01 to 6.11: Principles Related to Summary Tables o 7.01 to 7.13: Principles Related to Graphics
Formats
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DP's.
Planned and Actual Time
• Reporting for tables, figures and formal statistical analyses: o Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated. o The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate. • Reporting for Data Listings: o Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1). o Unscheduled or unplanned readings will be presented within the subject's listings. o Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures, summaries and statistical analyses.
Unscheduled Visits
• Unscheduled visits will not be included in summary tables. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.

Reporting Standard	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL Statistical Principle 6.06.1 Assign zero to NQ values (Refer to GUI_51487 for further details)
Reporting of Pharmacokinetic Parameters	
Descriptive Summary Statistics. (Un-Transformed)	N, n, arithmetic mean, 95% confidence interval (CI) for the arithmetic mean, SD, median, minimum, maximum and CV(%) • CV(%)=(SD/mean)*100
Descriptive Summary Statistics. (Log_e Transformed)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and between-subject geometric coefficient of variation (CVb (%)) will be reported. • Geometric mean = exp (mean on log_e scale) • CVb (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 [NOTE: SD = SD of log_e transformed data]
Parameters Not Being Log_e Transformed	Tmax
Listings	Include PK Parameters: Cmax, Tmax, Cτ, AUC(0-τ), t1/2 and CL/F.
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

10.6. Appendix 6: Derived and Transformed Data

10.6.1. General

Multiple Measurements at One Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented.
Study Day

• Calculated as the number of days from Treatment start date :
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < Treatment start Date → Study Day = Ref Date – Treatment start Date
  • Ref Data ≥ Treatment start Date → Study Day = (Ref Date – Treatment start Date) + 1

10.6.2. Study Population

Demographics
Age
• GSK standard IDSL algorithms will be used for calculating age using date of the screening visit relative to birth date, where birth date is imputed as: • Any subject with a missing date and month will have this imputed as '30th June'. • Birth date will be presented in listings as 'YYYY'.
Body Mass Index (BMI)
• Calculated as **Weight (kg) / [Height (m)]^2**

Extent of Exposure
• Number of days of exposure to study drug will be calculated based on the formula: **Duration of Exposure in Days = Treatment Stop Date – (Treatment Start Date) + 1**

10.6.3. Safety

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

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. • Example 1: 2 Significant Digits = '< x ' becomes x – 0.01 • Example 2: 1 Significant Digit = '> x' becomes x + 0.1 • Example 3: 0 Significant Digits = '< x' becomes x – 1

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

10.7.1. Premature Withdrawals

Element	Reporting Detail
General	All subjects who withdraw prematurely from the study/study drug will be documented, listed with the reason for their withdrawal recorded in the final Clinical Pharmacology Study Report (CPSR).

10.7.2. Handling of Missing Data

Element	Reporting Detail
General	Missing PK and safety data will not be imputed
Outliers	Any subjects excluded from the summaries and/or statistical analyses will be documented and flagged in the dataset and listing along with the reason for exclusion in the clinical study report.

10.7.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.
Adverse Events	The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: o Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 4: Treatment States and Phases. o Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. o Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.

10.7.2.2. Handling of PK Concentration Data

Element	Reporting Detail
General	If a PK sample in a profile is ‘no result’, ‘no sample received’, or ‘insufficient sample’, data will be set as missing. No imputation will be applied.

10.8. Appendix 8: Values of Potential Clinical Importance

10.8.1. Laboratory Values

Division of AIDS (DAIDS, Version 2.0, November 2014) AE grade 2 and above of lab abnormalities will be listed by subject, period/treatment, visit, and actual date and time.

Statistics and Programming group will use this version to add toxicity grades values in the ADAM dataset.

10.8.2. ECG

ECG Values of Potential Clinical Importance (Healthy Volunteers)

ECG Parameter	Potential Clinical Importance Range (PCI)	Unit
Absolute QTc Interval	>450	msec
Increase from baseline QTc	>60	msec
PR Interval	<110 and >220	msec
QRS Interval	<75 and >110	msec

10.8.3. Vital Signs

Vital Signs Values of Potential Clinical Importance (Healthy Volunteers)

Parameter	Potential Clinical Importance Range (PCI)	Unit
Systolic Blood Pressure	<85 and >160	mmHg
Diastolic Blood Pressure	<45 and >100	mmHg
Heart Rate	<40 and >110	bpm

10.9. Appendix 9: Model Specifications for Statistical Analysis

10.9.1. Statistical Analysis Assumptions and Model Specifications

Endpoint(s)	Cmax, Cτ , AUC(0-τ), t1/2 and CL/F, if data permitted
Analysis	Linear Mixed Model

Specifications:

- For the Linear Mixed Model, model assumptions will be PK parameter following log-normal distribution.
- For drug-drug interaction assessment, an example of SAS code is included here.

```
Proc Mixed;
      By parameter;
      class treatment subject;
      model logPKpar = treatment/ddfm=kr outpred=pred;
      random subject;
      lsmeans treatment;
      estimate 'B:A' treatment -1 1/cl alpha=0.1;
         /* (CAB+RTB) vs (CAB alone)*/
    run;
```

- An example of SAS code to assess achievement of steady-state is included here.

```
Proc Mixed;
    by dose;
    where day in (13,14);
    class subject;
    model logC0 = day/ddfm=kr cl alpha=0.1 solution;
    random intercept/subject=subject type=un solution;
    make 'solutionf' output=stat;
run;
```

repeat for Days 26,27,28 and Days 27,28

10.10. Appendix 10 - Abbreviations & Trade Marks

10.10.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
ADaM IG	Analysis Data Model Implementation Guide
AE	Adverse Event
ANOVA	Analysis of Variance
AUC	Area under concentration-time curve
AUC(0-τ)	Area under the concentration-time curve over one dosing interval
BESM	Bioanalytical External Study Monitors
BIB	Bioanalysis, Immunogenicity and Biomarkers
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CL/F	The apparent oral clearance
Cmax	Maximum observed concentration
CP	Clinical Programming
CPMS	Clinical Pharmacology Modelling & Simulation
CPSSO	Clinical Pharmacology Sciences and Study Operations
CRF	Case record form
CS	Clinical Statistics
Ct	Concentration at the end of the dosing interval
CV	Coefficient of Variation
CVb/CVw	Coefficient of Variation (Between)/Coefficient of Variation (Within)
DAIDS	Division of Acquired Immune Deficiency Syndrome
DBF	Database Freeze
DBR	Database Release
GSK	GlaxoSmithKline
HARP	Harmonized Analysis and Reporting Process
IDSL	Integrated Data Standards Library
LLQ	Lower limit of quantification
NC	Not Calculable
NQ	Non-quantifiable concentration measured as below LLQ
PK	Pharmacokinetic
QSci	Quantitative Sciences
RAP	Reporting and Analysis Plan
RBT	Rifabutin
RTF	Rich Text Format
SAS	Statistical Analysis System
SD	Standard deviation
SDTM	Study Data Tabulation Model
SRP	Statistics Resourcing and Programming
t½	Terminal phase half-life
Tmax	Time of occurrence of Cmax

10.10.2. Trademarks

Trademarks of ViiV Healthcare
NONE

Trademarks not owned by ViiV Healthcare
Mycobutin
SAS
WinNonlin

10.11. Appendix 11: List of Data Displays

10.11.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.n	N/A
Safety	2.1 to 2.n	N/A
Pharmacokinetic	3.1 to 3.n	3.1 to 3.n
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	x+1 to y	

10.11.2. Mock Example Referencing

All displays will be provided with an example from previous CAB studies LAI117010 and LAI117011 or mock examples are provided.

10.11.3. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Safety	LAI117010/ Table 1.1	Summary of Analysis Populations	by Overall	SAC
1.2.	Safety	LAI117010/ Table 1.2	Summary of End of Study Record by Treatment and Overall	By subject and treatment	SAC
1.3.	Safety	LAI117010/ Table 1.3	Listing of End of Study Record	By subject	SAC
Demographics and Enrolment Information					
1.4.	Safety	LAI117010/ Table 1.5	Summary of Demographic characteristics	Include BMI, Race detail	SAC
1.5.	Safety	LAI117010/ Table 1.6	Summary of Race for Safety Population	By treatment and Overall	SAC
1.6.	Safety	LAI117010/ Table 1.7	Listing of Concomitant Medication	By Subject. Change from listing to summary if more than 3 pages	SAC
1.7.	Safety	LAI117010/ Table 1.8	Listing of Genetics Subject Accountability		SAC
1.8.	Safety	LAI117010/ Table 1.9	Listing of Treatment Non-Compliance		SAC
1.9.	Safety	LAI117010/Table 1.10	Listing of Subjects with Protocol Deviations		SAC
1.10.	Safety	LAI117010/Table 1.11	Summary of Screening Information		SAC
1.11.	Safety	LAI117011/Table 1.11	Age Group Breakdown for the Trial	For Eudra posting	

10.11.4. Safety Tables

Safety Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
2.1.	Safety	LAI117010/ Table 2.1	Summary of Exposure Data	By subject and treatment	SAC
2.2.	Safety	LAI117010/ Table 2.2	Relationship of Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text		SAC
2.3.	Safety	LAI117010/ Table 2.3	Summary of All Adverse Events by Treatment		SAC
2.4.	Safety	LAI117010/ Table 2.4	Summary of Drug-Related Adverse Events by Treatment		SAC
2.5.	Safety	LAI117010/ Table 2.5	Listing of Serious Adverse Events	By subject and treatment.	SAC
2.6.	Safety	LAI117010/ Table 2.6	Listing of Adverse Events Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study	By subject and treatment	SAC
Labs					
2.7.	Safety	LAI117010/ Table 2.7	Listing of Reference Ranges for Clinical Laboratory Tests		SAC
2.8.	Safety	LAI117010/ Table 2.8	Summary of Clinical Haematology Laboratory Data by Treatment and Time		SAC
2.9.	Safety	LAI117010/ Table 2.9	Summary of Clinical Chemistry Laboratory Data by Treatment and Time		SAC
2.10.	Safety	LAI117010/ Table 2.10	Summary of Treatment Emergent Grade 2 or Higher Lab Abnormalities by Treatment	Summary of Treatment Emergent Lab toxicity only.	SAC
2.11.	Safety	LAI117010/ Table 2.11	Listing of Treatment Emergent Grade 2 or Higher Lab Abnormalities	By subject and treatment	SAC
2.12.	Safety	CP_LB5	Summary of All Urinalysis Data		SAC

Safety Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Vital Signs					
2.13.	Safety	LAI117010/ Table 2.13	Summary of Vital Signs by Treatment and Time	Include BP and HR only.	SAC
2.14.	Safety	LAI117010/ Table 2.14	Summary of Change from baseline in Vital Signs by Treatment and Time	Include BP and HR only.	SAC
2.15.	Safety	LAI117010/ Table 2.15	Listing of Vital Signs for Subjects with Abnormalities of Potential Clinical Importance	By subject and treatment	SAC
ECGs					
2.16.	Safety	LAI117010/ Table 2.16	Summary of ECG Findings		SAC
2.17.	Safety	LAI117010/ Table 2.17	Summary of ECG Values by Treatment and Time		SAC
2.18.	Safety	LAI117010/ Table 2.18	Summary of Change from Baseline in ECG Values by Treatment and Time		SAC
2.19.	Safety	LAI117010/ Table 2.19	Summary of Category of QTc Data by Treatment and Time		SAC
2.20.	Safety	LAI117010/ Table 2.20	Summary of Category of QTc Change from Baseline by Treatment and Time		SAC
2.21.	Safety	LAI117010/ Table 2.21	Listing of ECG Values for Subjects with Abnormalities of Potential Clinical Importance	By subject and treatment	SAC
2.22.	Safety	LAI117010/ Table 2.22	Listing of Clinically Significant ECG Abnormalities	List all data for a subject with clinically significant abnormalities	SAC
2.23.	Safety	LAI117011/Table 2.17	Summary of Serious Adverse Events by Preferred Term Including Drug-related Status and Fatal Status	Eudra posting table	SAC
2.24.	Safety	LAI117011/Table 2.18	Summary of Non-Serious Adverse Evens by Preferred Term with Occurrences >5%	Eudra posting table	SAC

Safety Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.25.	Safety	IDSL LIVER5	Listing of Liver Monitoring and stopping Event Reporting	IDSL standard for liver event	SAC

10.11.5. Pharmacokinetic Tables

Pharmacokinetic Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.1.	PK Summary	LAI117010/Table 3.1	Summary of CAB Plasma Concentration-time Data (unit) by Treatment	Treatments A, B	SAC
3.2.	PK Parameter	LAI117010/Table 3.2	Listing of Derived Plasma CAB PK Parameters	All parameters with units;	SAC
3.3.	PK Summary	LAI117010/Table 3.3	Summary of Derived Plasma CAB PK Parameters	All parameters with units	SAC
3.4.	PK Summary	LAI117010/Table 3.4	Listing of Individual Plasma CAB PK Parameter Treatment Ratios	For Cmax, AUC(0-τ), Cτ	SAC
Statistical Analysis Table					
3.5.	PK Summary	LAI117010/Table 3.5	Summary of Statistical Analysis of CAB Plasma PK Parameters Comparison		SAC
3.6.	PK Summary	ITZ112929/Table 11.9	Summary of Stead-State Assessment		SAC

10.11.6. Pharmacokinetic Figures

Pharmacokinetic Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.1.	PK Plasma Concentration	LAI117010/ Figure 3.1	Individual CAB Plasma Concentration-time Plot (Linear and Semi-log) by Subject	Paged by Subject	SAC
3.2.	PK Summary	LAI117010/ Figure 3.2	Median Plasma CAB Concentration-Time Plots by Treatment (Linear and Semi-Log)		SAC
3.3.	PK Summary	LAI117010/ Figure 3.3	Mean Plasma CAB Concentration-Time Plots by Treatment (Linear and Semi-Log)		SAC
3.4.	PK Summary	LAI117010/ Figure 3.4	Comparative Plot of Plasma CAB PK Parameters between Treatments	PK_F1 mock up	SAC
3.5.	PK Summary	LAI117010/ Figure 3.5	Geometric Mean Treatment Ratios and 90% CIs of CAB PK Parameters	PK_F2 mock up	SAC

10.11.7. ICH Listings

ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Randomisation					
1	Safety	CP_RA1x (XO)	Listing of Randomized and Actual Treatments	Add randomization date	SAC
Subject Disposition					
2	Screening	ES7	Listing of Reasons for Screening Failures	Include Age and Sex. Concatenate with Subjid	SAC
3	Safety	CP_ES10x (XO)	Listing of Reasons for Withdrawal		SAC
4	Safety	IE4 (XO)	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC
Demographics					
5	Safety	DM4 (XO)	Listing of Demographic Characteristics		SAC
6	Safety	DM10 (XO)	Listing of Race		SAC
Concomitant Medication					
7	Safety	CP_CM4 (XO)	Listing of Concomitant Medications by Generic Term		SAC
Exposure					
8	Safety	EX4 (XO)	Listing of Exposure Data		SAC

ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
9	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events		SAC
10	Safety	CP_AE9 (XO)	Listing of All Adverse Events		SAC
LABS					
11	Safety	CP_LB6 (xo)	Listing of Clinical Chemistry	Include all tests, toxicity grades and range flags	SAC
12	Safety	CP_LB6 (xo)	Listing of Hematology	Include all tests, toxicity grades and range flags	SAC
13	Safety	UR2b	Listing of Urinalysis Data		SAC
ECGs					
14	Safety	CP_EG4 (xo)	Listing of ECG Values of Potential Clinical Importance		SAC
15	Safety	CP_EG4 (xo)	Listing of All ECG Values for Subjects with any Value of Potential Clinical Importance		SAC
16	Safety	CP_EG6 (xo)	Listing of Abnormal ECG findings		SAC
Vital Signs					
17	Safety	CP_VS5 (XO)	Listing of Vital Signs of Potential Clinical Importance		SAC
18	Safety	CP_VS5 (XO)	Listing of All Vital Signs for Subjects with any Value of Potential Clinical Importance		SAC

10.11.8. Non-ICH Listings

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK					
19	PK Plasma Concentration	pkcl1x	Listing of CAB Plasma Concentration-time Data		SAC
20	PK Summary	N/A	SAS Output from Statistical Analysis of Log_e-transformed CAB Plasma PK Parameters of Treatment Comparison		SAC

10.12. Appendix 12: Example Mock Shells for Data Displays

10.12.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Example : PK_T1
Protocol : 205712 Page 1 of n
Population : PK Parameter Summary

Table xx.xx
Summary of Statistical Analysis of Log_e-transformed CAB Plasma Pharmacokinetic Parameters based on Actual Sampling Time

Parameter	*Comparison Test vs Reference*	*Adjusted Geometric Mean n Test*	*n Ref*	*Ratio (Test/Ref)*	*90% Confidence Interval for Ratio*	*%CVw*
Cmax(units)	*[Test treatment description] vs [Reference treatment description]*	*x xx.xx*	*x xx.xx*	*x.xxxx*	*(x.xxxx, x.xxxx)*	*xx.x*
AUC(0-τ)(units)	*[Test treatment description] vs [Reference treatment description]*	*x xx.xx*	*x xx.xx*	*x.xxxx*	*(x.xxxx, x.xxxx)*	*xx.x*
Cτ(units)	*[Test treatment description] vs [Reference treatment description]*	*x xx.xx*	*x xx.xx*	*x.xxxx*	*(x.xxxx, x.xxxx)*	*xx.x*

Example LIVER5
Protocol: XYZ100001
Population: Intent-to-Treat/Safety/Other study specific (Data as of: 30MAY2011)

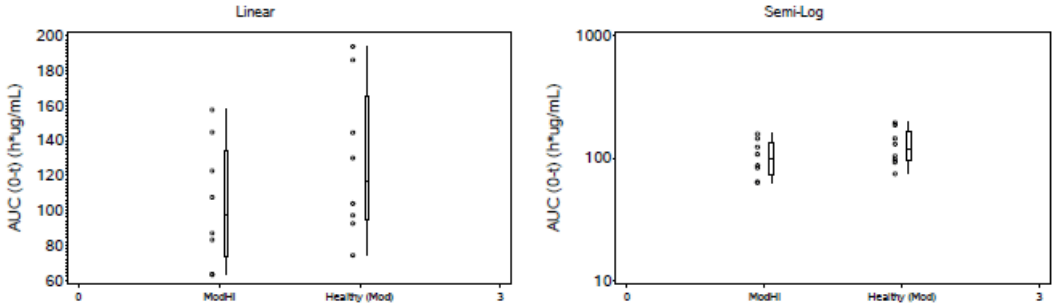
Listing X
Listing of Liver Monitoring/Stopping Event Reporting

Treatment: Treatment A

Site Id./ Unique Subject Id.	Age(YEARS)/ Sex/ Race Detail	Maximum Status of the Liver Event	Date First Detected/ Study Day	Time Since First Dose (days)	Time Since Last Dose (days)	Restart/Re-challenge After Stopping Criteria Was Met	Resolved?/ Date resolved
PPD	63/ M/ WHITE - WHITE/CAUSASIAN/EUROPEAN HERITAGE	LIVER MONITORING CRITERIA	PPD 101	101	1	N	Y/ 2010-02-19
PPD	61/ F/ ASIAN - JAPANESE HERITAGE	LIVER EVENT STOPPING CRITERIA	PPD 68	68	1	Y	Y/ 2010-04-10
		LIVER EVENT STOPPING CRITERIA	PPD 134	134	7	N	N

Example : PK_*F1*
Protocol : *205712*
Population : PK Summary

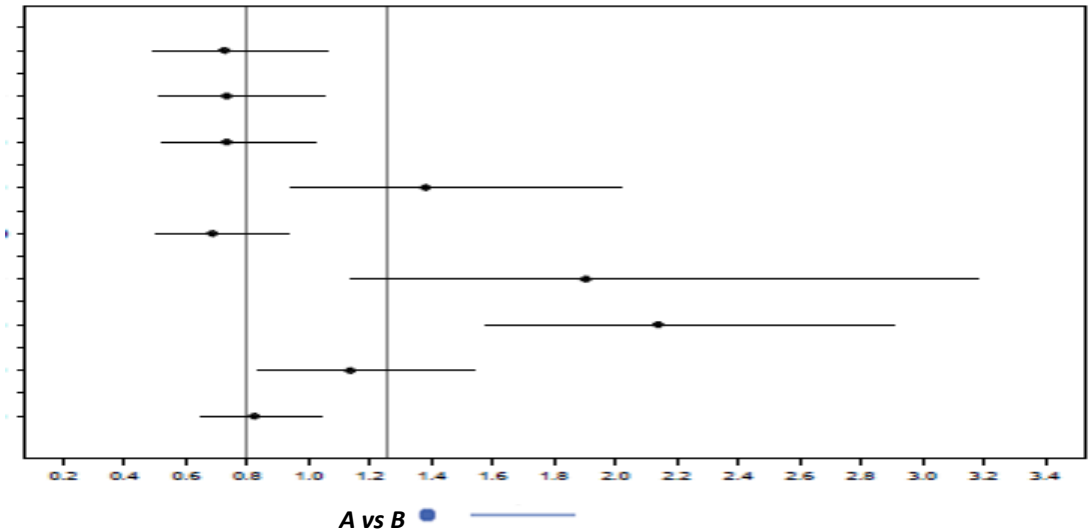
Figure xx.xx
Box Plot of Plasma Comparative of Geometric Mean (95% CI) with Individual Subjects
CAB Pharmacokinetic Parameters



Programming note: add footnote for treatment A, B.

Example : PK_F2 Page 1 of n
Protocol : 205712
Population : PK Parameter Summary

Figure xx.xx
Geometric Mean Treatment Ratio and 90% CI of CAB Plasma Pharmacokinetic Parameters



Note: The reference lines are at ratios of 0.80, 1.25.

Programming note: add footnote for treatment A, B.