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

Title	:	Reporting and Analysis Plan for a randomized open-label relative bioavailability study to compare the pharmacokinetic parameters of a lower dose formulation of ambrisentan (GSK1325760) with marketed ambrisentan in healthy adult participants
Compound Number	:	GSK1325760
Effective Date	:	14-JAN-2020

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 205019
- This RAP is intended to describe the analyses for primary and secondary endpoints 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):

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Approver	Date
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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 2017N346964_00.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

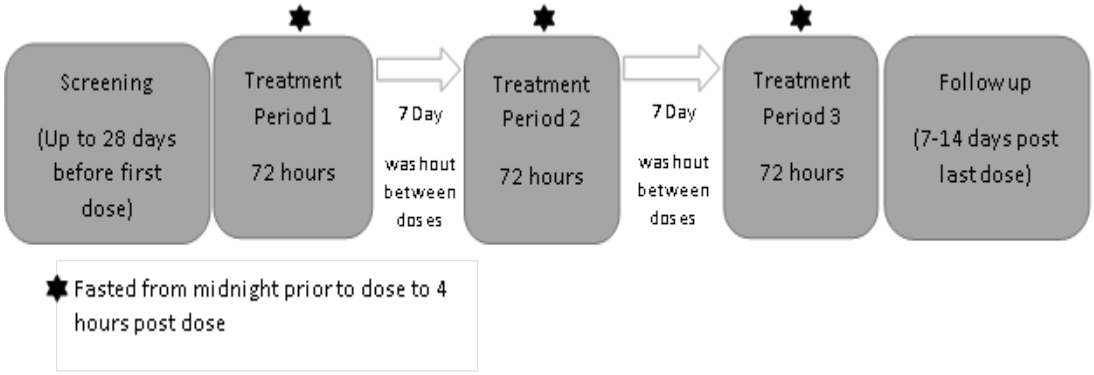
There were no changes or deviations to the originally planned statistical analysis specified in the protocol (Dated: 21/Jun/2019).

Note: Although all PK parameters are included in the primary endpoints, only AUC and Cmax will be analysed by statistics in line with success definition in the protocol and the rest PK parameters will be reported and treated as of secondary importance.

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

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To compare the relative bioavailability of Ambrisentan (AMB 1 mg x 5 tablets) administered as tablets dispersed in water or administered orally, with marketed Ambrisentan (AMB 5 mg x 1 tablet) in healthy adult participants under fasted conditions	• Plasma pharmacokinetic parameters of AMB as data permits: Maximum observed plasma concentration (C_{max}), Time to Cmax (t_{max}), Area under concentration-time curve from time zero (predose) extrapolated to infinite time($AUC_{(0-\infty)}$), area under the concentration-time curve from time zero (predose) to last time of quantifiable concentration $AUC_{(0-t)}$ and Terminal phase half-life ($t_{½}$), time of last quantifiable concentration (t_{last})
Secondary Objectives	**Secondary Endpoints**
• To monitor the safety and tolerability of Ambrisentan (AMB 1 mg x 5 tablets) administered as tablets dispersed in water or administered orally, compared with marketed Ambrisentan (AMB 5 mg x 1 tablet) administered orally, in healthy adult	• Adverse events (AE), vital signs, electrocardiogram (ECG), and clinical laboratory values.
Exploratory Objectives	**Exploratory Endpoints**
• To investigate palatability of AMB (1 mg x 5 tablets) dispersed in water, in healthy adult participants.	• Palatability questionnaire scores

2.3. Study Design

Overview of Study Design and Key Features	
	
Design Features	This is a single centre, open-label, randomised, single dose, 3-period cross over study in healthy participants to compare the PK of a new lower dose formulation AMB tablet (dispersed in water and administered orally) with the reference marketed AMB tablet (administered orally) Each participant will have 3 treatment periods (single oral doses) in a treatment sequence in which subjects will be randomised to one of the following study interventions in each treatment period: • **Test 1 (F1):** 5 mg (5 x 1 mg tablets) AMB tablet dispersed in water • **Test 2 (F2):** 5 mg (5 x 1 mg tablets) AMB tablet administered orally • **Reference (R):** 5 mg (1 x 5 mg tablet) AMB tablet administered orally Each participant will: • be screened (within 28 days of their first dose) • have 3 treatment periods (3 overnight clinic stays, and 1 out-patient visit per treatment period. A minimum of 7 days between doses in each treatment period); and • have a follow-up visit (within 7 to 14 days after their last dose)
Dosing	The investigational drug is GSK1325760(AMB) Each participant will have 3 treatment periods and will be randomised to one of the study interventions in each period: • **Test 1 (F1):** 5 mg (5 x 1 mg tablets) AMB tablet dispersed in water • **Test 2 (F2):** 5 mg (5 x 1 mg tablets) AMB tablet administered orally • **Reference (R):** 5 mg (1 x 5 mg tablet) AMB tablet administered orally Palatability Questionnaire only to be completed in the Treatment Period dosing AMB tablets dispersed in water. To be completed within 10 min of dosing.
Time & Events	• Refer to Appendix 2: Schedule of Activities
Treatment Assignment	• This is an open label study and each participant will have 3 treatment periods (single oral doses) in a treatment sequence in which subjects will be randomised to one of the study interventions in each treatment period
Interim Analysis	• No Interim analysis will be performed in this study

2.4. Statistical Hypotheses / Statistical Analyses

This is an investigative study to study the pharmacokinetic parameters of a new formulation of AMB. Due to its descriptive nature, there will be no formal statistical hypothesis tested.

An estimation approach will be used to i) estimate the bioavailability of the test formulation relative to the reference formulation, and ii) for AUC (0-inf), AUC(0-t) and Cmax, point estimates and corresponding 90% confidence intervals will be constructed for the ratio of the geometric mean of the test formulation to the geometric mean of the reference formulation.

3. PLANNED ANALYSES

3.1. Interim Analyses

No Interim Analysis is planned for this study

3.2. Final Analyses

The final planned primary analyses will be performed after the completion of the following sequential steps:

1. All participants have completed the study as defined in the protocol.
2. All required database cleaning activities have been completed and final database release (DBR) and database freeze (DBF) has been declared by Data Management.
3. Randomization codes have been distributed according to RandAll NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants who were screened for eligibility	• Screen failures
Randomized	• All participants who were randomly assigned to treatment in the study. • This population will be based on the treatment the participant was randomized to.	• Study Population
Safety	• All randomized participants who take at least 1 dose of study intervention. Participants will be analysed according to the intervention they actually received.	• Safety Population
Pharmacokinetic Concentration (PK)	• The PK Concentration Population will include all participants for whom at least one PK sample was obtained and analysed.	• PK
Pharmacokinetic Parameter (PK_PAR)	• For each PK parameter, the PK Parameter Population will include all participants who provide PK parameter data.	• PK_PAR

Refer to Appendix 10: List of Data Displays which details the population used for each display.

4.1. Protocol Deviations

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

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan final version, 27-SEP-2019.

- Data will be reviewed prior to Database Release (DBR) to ensure all important deviations 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 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. Study Treatment & Sub-group Display Descriptors

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

Treatment Group Descriptions			
RandAll NG		**Data Displays for Reporting**	
Code	**Description**	**Description**	**Order in TLF**
F1	GSK1325760 5 mg dispersed in water	Dispersed GSK1325760	1
F2	GSK1325760 5 mg administered orally	Oral GSK1325760	2
R	Marketed AMB	Marketed AMB	3

1. Dispersed GSK1325760 vs Marketed AMB (F1 vs R)
2. Oral GSK1325760 vs Marketed AMB (F2 vs R)

Note: Relevant footnotes to be added in all the displays as:

Dispersed GSK1325760: 5 mg (5 x 1 mg tablets) AMB tablet dispersed in water

Oral GSK1325760: 5 mg (5 x 1 mg tablets) AMB tablet administered orally

Marketed AMB: 5 mg (1 x 5 mg tablet) AMB tablet administered orally

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment with a non-missing value.If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline.

Parameter	Study Assessments Considered as Baseline			Baseline Used in Data Display
	Screening	Day -1	Day 1 (Pre-Dose)	
Safety				
Vital Signs	X[1]		X[1]	Day 1 (mean of the pre-dose)[2]
ECG	X[1]		X[1]	Day 1 (worst case pre-dose)[2]
Haematology+ Clinical Chemistry + Urinalysis[3]	X	X		Day-1

NOTES:

[1] Taken in triplicate

[2] Worst case of the triplicate pre-dose assessments for ECG will be the maximum value of the three measurements for each of the ECG parameter and mean of the pre-dose for Vital signs

[3] Urinalysis baseline value required only when microscopic examination done

6. STUDY POPULATION ANALYSES

6.1. Other Considerations for Data Analyses and Data Handling Conventions

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

Section	Component
10.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
10.5	Appendix 5: Data Display Standards & Handling Conventions
10.6	Appendix 6: Derived and Transformed Data
10.7	Appendix 7: Reporting Standards for Missing Data
10.8	Appendix 8: Values of Potential Clinical Importance

6.2. Overview of Planned Study Population Analyses

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

Study population analyses including analyses of subject's disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, and exposure and treatment compliance will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 10: List of Data Displays.

7. SAFETY ANALYSES

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

7.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs) will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 10: List of Data Displays.

7.2. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Hematology laboratory tests, Urinalysis, and liver function tests will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 10: List of Data Displays.

7.3. Other Safety Analyses

The analyses of non-laboratory safety test results including ECGs and vital signs will be based on GSK Core Data Standards, unless otherwise specified. The details of the planned displays are presented in Appendix 10: List of Data Displays.

8. PHARMACOKINETIC ANALYSES

8.1. Primary Pharmacokinetic Analyses

The pharmacokinetic (PK) analyses will be based on the "Pharmacokinetic Concentration (PK)" population, unless otherwise specified.

Table below provides an overview of the planned analysis, with the full details being presented in Appendix 10: List of Data Displays:

Display Type	Untransformed							Ln-Transformed						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
PK Concentrations				Y	Y[1] [2]	Y[1]	Y							
Plasma PK Parameters	Y			Y	Y[1]	Y	Y			Y	Y			

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual participant observed raw data.

1. [1] Linear and Semi-Logarithmic plots will be created on the same display.
2. [2] Separate mean and median plots will be generated.

8.1.1. Endpoint / Variables

8.1.1.1. Drug Concentration Measures

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

Concentrations of ambrisentan in plasma will be listed and summarised by treatment and actual time.

Standard summary statistics will be calculated (i.e. arithmetic mean, standard deviation, median, minimum and maximum).

Refer to the PK Guidance document, titled Non-Compartmental Analysis of Pharmacokinetic Data (GUI_51487) for more information regarding the treatment of concentrations below the assay's lower limit of quantification (NQ).

Individual plasma concentration-time profiles and median/mean profiles by treatment will be plotted. Each of the figures will contain one plot on the untransformed scale (i.e. a linear plot) and one plot on the loge-transformed scale (i.e., log-linear plot). In addition, a plot showing all individual subjects for each treatment will be produced (both linear and log-linear).

8.1.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin [version 8.1 or above]. All

calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters will be determined from the plasma concentration-time data, as data permits, for each subject and treatment unless otherwise specified. If parameters cannot be determined, a flag will be present in the data.

Parameter	Parameter Description
AUC(0-t)	Area under the concentration-time curve from time zero to the time of the last quantifiable concentration (C(t)) will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC(0-inf)	Area under the concentration-time curve extrapolated to infinity will be calculated as: AUC(0-inf) = AUC(0-t) + Ct / lambda_z where Ct is the last observed quantifiable concentration.
Cmax	Maximum observed concentration determined directly from the concentration-time data.
Tmax	Time to reach Cmax, determined directly from the concentration-time data.
t1/2*	Apparent terminal half-life will be calculated as: t1/2 = ln2 / lambda_z
%AUCext	The percentage of AUC(0-∞) obtained by extrapolation (%AUCex) will be calculated as: [AUC(0-∞) – AUC(0-t)] / AUC(0-∞) x 100
Ct	The last observed quantifiable concentration
Tlast	Time of last quantifiable concentration

* associated parameters lambda_z, lambda_z_lower, lambda_x_upper, No_points_lambda_z to be listed.

NOTES:

Additional parameters may be included as required.

Lambda_z is the terminal phase rate constant.

Derived pharmacokinetic parameters will be listed by subject and treatment. Listings will also include the individual subject ratios for AUC(0-inf), AUC (0-t) and Cmax, and the first point, last point and number of points used in the determination of λz.

8.1.2. Summary Measure

- For each of the parameters AUC (0-inf), AUC (0-t), t1/2 and Cmax, the following summary statistics will be calculated and tabulated by treatment:
  - **Untransformed Data** : N, n, arithmetic mean, 95% confidence interval (CI) for the arithmetic mean, SD, median, minimum, maximum
  - **Loge-transformed Data**: Geometric mean, 95% CI for the geometric mean, SD of loge-transformed data and %CVb

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

  As per the intercurrent events observed as defined in Section 8.1.3, relevant datapoints will be excluded from the pharmacokinetic parameters summary tables.

  - Relative bioavailability of the new formulation of AMB and referenced or marketed AMB will be analysed by using AUC(0-t), AUC (0-∞), Cmax parameters

8.1.3. Strategy for Intercurrent (Post Randomization) Events

Participants who experienced the following intercurrent events will have data from the relevant treatment period excluded from analysis:

- Did not receive full dosing
- Had a vomit within the first 2.5 hours after dose completion
- Did not provide an adequate PK concentration profile to allow reliable estimation of PK parameters

8.1.4. Population of Interest

The primary statistical analyses will be based on the Pharmacokinetic parameter population (PK_PAR), unless otherwise specified.

8.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 10: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 8.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

8.1.5.1. Statistical Methodology Specification

The following pharmacokinetic statistical analyses will only be performed if sufficient data is available (i.e. if subjects have well defined plasma profiles).

Endpoint / Variables
• Log_e-transformed $AUC_{(0-t)}$, $AUC_{(0-\infty)}$, C_{max} PK parameters of test formulation of GSK1325760 (F1, F2) and marketed AMB (R)
Model Specification

• Will be statistically analyzed separately using a mixed model (MM) for all treatment periods
• Terms fitted in the mixed effect ANOVA model will include:
  ○ Fixed Effect: Treatment (F1, F2, R), Treatment Period
  ○ Random Effect: Subject
• The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used
• Point estimates for the adjusted means on the log_e scale, the mean difference between treatments and associated 90% confidence interval for the contrast (test-reference) will be constructed using the residual variance for the following differences of interest:
  ○ AMB (1 mg x 5 tablets) administered as tablets dispersed in water(F1) and administered orally(F2) versus marketed AMB (R)(5 mg x 1 tablet) administered orally
• As per the observed intercurrent events, the strategy in sec 8.1.3 will be followed to exclude data points following the definition of intercurrent events

Model Checking & Diagnostics
For the Mixed Model analysis, Model assumptions will be applied, but appropriate adjustments may be made based on the data. • Distributional assumptions underlying the model used for analysis will be examined by obtaining a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable. • If there are any departures from the distributional assumptions, alternative transformations, such as data squared, or square root of data, will be explored

Model Results Presentation
• The point estimate and confidence interval obtained from MM analysis will be exponentially back-transformed to obtain Adjusted (least square) geometric means for each treatment • Point estimates (Relative Bioavailability of GSK1325760) and associated 90% confidence interval for the ratio F1/R and F2/R along with within-subject variability ($\%CV_w$) will be reported Where $\%CV_w=100*(SQRT\ (EXP(\sigma_w^2)-1))$ and σ_w^2 is the mean squares error (MSE) from the statistical Mixed model • Geometric Mean along with 90% CI treatment Ratios of GSK1325760 Plasma Derived Pharmacokinetic Parameters will also be plotted as in Section 10.10.8

9. REFERENCES

GlaxoSmithKline Document Number 2017N346964_00: An open-label, randomized three period cross-over relative bioavailability study to compare the pharmacokinetic parameters of a lower dose formulation of ambrisentan (GSK1325760) with marketed ambrisentan in healthy adult participants.

10. APPENDICES

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

A Per Protocol Population is not being defined for this study. Please Refer to Section 4.1 for handling and Reporting of Protocol Deviations.

10.2. Appendix 2: Schedule of Activities

10.2.1. Protocol Defined Schedule of Events

10.2.2. Screening and Follow-up Schedule of Events

Procedure	Screening[1] (up to 28 days before first dose)	Follow up/Early Withdrawal (7-14 days post last dose)	Notes
Informed consent	X		
Inclusion and exclusion criteria	X		
Demography	X		
Medical history (includes substance usage)	X		Substances: Drugs, Alcohol, tobacco
Full physical exam, including height and weight	X		
Brief physical exam		X	
HIV, Hep B and Hep C screen	X		
Clinical chemistry, haematology and urinalysis	X	X	Only screening tests need to be fasted
FSH	X		Required only in women to confirm postmenopausal status
Alcohol breath test	X		
Urine or serum drugs test	X		
Vital signs (blood pressure, heart rate and temperature)	X	X	Triplicate blood pressure and heart rate required at screening.
12-lead ECG	X	X	Triplicate ECG required at screening.
Concomitant Medication review	X	X	Con meds before dosing can be recorded in medical history
AE/SAE review	X	X	Refer to protocol Section 8.3.1

1. Screening assessments may be conducted at multiple visits, if required.

10.2.3. Treatment Periods 1, 2 and 3 (minimum of 7 days washout between doses)

Procedure	Day –1	Day 1 (hours)											Day 2		Day 3	Day 4	Notes
		Pre-dose	0	0.5	1	1.5	2	2.5	4	8	12	18	24	36	48	72	
Clinic Visits																	
Out-patient Visit																X	
Admission to clinic	X																
Discharge from clinic															X		If more convenient for participants, they can remain in the unit until 72 h, at the discretion of the investigator
Study Intervention																	
Randomisation		X															Can be done on Day –1 or Pre-dose Day 1. Only in Treatment Period 1
Study Intervention			X														Fasted from midnight until 4 h afterwards, except for water, allowed ad libitum, except for 1 h before and after dosing
Safety Assessments																	
Vital signs (blood pressure, heart rate and temperature)		X		X	X		X		X	X	X		X		X	X	Triplicate pre-dose. Single measurements at other timepoints, unless out of range, then triplicates should be performed
12-lead ECG		X			X		X		X		X		X			X	
Clinical chemistry, haematology and urinalysis	X														X		Fasting not required
Brief physical examination	X																

Procedure	Day –1	Day 1 (hours)											Day 2		Day 3	Day 4	Notes
		Pre-dose	0	0.5	1	1.5	2	2.5	4	8	12	18	24	36	48	72	
Alcohol breath test	X																
Urine or serum drugs test	X																
Concomitant Medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	Con meds before dosing can be recorded in medical history
SAE/AE review	◄==========►																Refer to Protocol Section 8.3.1
Other Assessments																	
PK blood samples		X		X	X	X	X	X	X	X	X	X	X	X	X	X	
Platability Questionnaire			X														Questionnaire only to be completed in the Treatment Period dosing AMB tablets dispersed in water. To be completed within 10 min of dosing

- When scheduled at the same time-points, 12-lead ECGs and vital signs should be completed before any blood draws.
- The timing of assessments should allow PK samples to be taken as close as possible to the nominal time-point.
- The timing and number of planned safety assessments and pharmacokinetic samples may be altered during the course of the study based on newly available data (e.g., to obtain data closer to the time of peak plasma concentrations) to ensure appropriate monitoring.
- Any changes in the timing or addition of time points for any planned study assessments as the result of emerging pharmacokinetic data from this study must be documented and approved by the relevant study team member and then archived in the sponsor and site study files but will not constitute a protocol amendment. The Competent Authority (CA) and ethics committee (EC) will be informed of any safety issues that constitute a substantial amendment and require alteration of the safety monitoring scheme or amendment of the informed consent form (ICF). The changes will be approved by the CA and the EC before implementation.

10.3. Appendix 3: Assessment Windows

Required assessment windows are specified in the Study Reference Manual for this study.

10.4. Appendix 4: Study Phases and Treatment Emergent Adverse Events

10.4.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to study treatment.

10.4.1.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is before 28 days prior to screening visit
Concomitant	Any medication that is not a prior, and up to the last scheduled visit

NOTES:

- Please refer to Appendix 7: 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.

10.4.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	• If AE onset date is on or after treatment start date & on or before treatment stop date. (plus, washout or protocol-specified time limit (e.g. half-life of drug, certain number of days, etc.). • Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date+ 1 day • If AE onset is during one period and worsens during a later period it would be counted in both periods. For the initial period the logic would be as above. For the later period the logic would use the treatment dates associated with the later period: Treatment Period Start Date ≤ AE Worsening Date ≤ Study Treatment Stop Date+ 1 day

NOTES:

- If the study treatment stop date is missing, then the AE will be considered to be On-Treatment.
- Time of study treatment dosing and start/stop time of AEs should be considered, if collected.

10.5. Appendix 5: Data Display Standards & Handling Conventions

10.5.1. Reporting Process

Software	
• The SAS Version 9.4 or above and WinNonlin Version 8.1 or above will be used.	
Reporting Area	
HARP Server	: uk1salx00175
HARP Compound	: dmwork/gsk1325760/mid205019
Analysis Datasets	
• Analysis datasets will be created according to latest IDSL	
Generation of RTF Files	
• RTF files will be generated for final SAC	

10.5.2. Reporting Standards

General	

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

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

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

Unscheduled Visits	
• Unscheduled visits will not be included in summary tables and/or figures. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %

Graphical Displays
• Refer to IDSL Statistical Principals 7.01 to 7.13.

10.5.3. Reporting Standards for Pharmacokinetic

Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL PK Display Standards. Refer to IDSL Statistical Principle 6.06.1. Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.
Reporting of Pharmacokinetic Parameters	
Descriptive Summary Statistics (Log Transformed)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and between and or within geometric coefficient of variation (CVb/w (%)) will be reported. [1] CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of log transformed data) [2] CV_w (%) = $\sqrt{}$ (exp(MSE) - 1) * 100 (MSE = mean square error from mixed effect model of loge-transformed data).
Parameters Not Being Log Transformed	T_{max}, T_{last}, first point, last point, and number of points used in the determination of λz, %AUCex
Summary Tables	All provided PK parameters will be summarised except Lamz, lamzUL, LamzLL, LamzNP and AUC % extrapolated area , Rsq-adjusted (if calculated).
Listings	Additionally, include the first point, last point and number of points used in the determination of lambda_z for listings.

10.6. Appendix 6: Derived and Transformed Data

10.6.1. General

Multiple Measurements at One Analysis 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. • Participants having both High and Low values for Normal Ranges at any post-baseline visit for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

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

Palatability Questionnaire
• Time difference between dose and questionnaire will be derived as: Date/time of assessment - Date/time of dose If this difference <= 10 min, then this subject will be flagged as Y else N A separate flag variable for particularly this treatment will record value as Y or N

10.6.2. Study Population

Demographics
Age
• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows: • Since Year of Birth is recorded in eCRF, date and month will be imputed as '30th June' of that Year. • 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** • Participants who were randomized but did not report a treatment start date will be categorised as having zero days of exposure.

10.6.3. Safety

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 decimal places 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 Decimal Places = '< x' becomes x – 0.01 • Example 2: 1 Decimal Places = '> x' becomes x + 0.1 • Example 3: 0 Decimal Places = '< x' becomes x – 1
Adverse Events
AE'S OF Special Interest
• Not Applicable

ECG Parameters
• Machine read values of PR, QRS, QT, QTc, QTcB, QTcF will be captured

10.6.4. Pharmacokinetic

PK Endpoints
• Not required in this section, please refer Section 8.1

10.7. Appendix 7: Reporting Standards for Missing Data

10.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion (i.e. as specified in the protocol) was defined as A participant is considered to have completed the study if he/she has completed all phases of the study including the follow-up visit. • Withdrawn participants will not be replaced in the study. • All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified. • Withdrawal visits will be summarised as withdrawal visits.

10.7.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: o These data will be indicated by the use of a "blank" in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. o 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.

10.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: 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: Study Phases and Treatment Emergent Adverse Events. 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. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.
Concomitant Medications/	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention:

Element	Reporting Detail
Medical History	○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month ○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

10.8. Appendix 8: Values of Potential Clinical Importance

10.8.1. Laboratory Values

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Hematocrit	Ratio of 1	Male		0.54
		Female		0.54
		Δ from BL	> 0.075	
Haemoglobin	g/L	Male		180
		Female		180
		Δ from BL	>25	
Lymphocytes	$x10^9$/ L		0.8	
Neutrophil Count	$x10^9$/ L		1.5	
Platelet Count	$x10^9$/ L		100	550
While Blood Cell Count (WBC)	$x10^9$/ L		3	20

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Albumin	g/L		30	
Calcium	mmol/L		2	2.75
Creatinine	umol/L	Δ from BL		>44.2
Glucose (fasting at screening)	mmol/L		3	9
Magnesium	mmol/L		0.5	1.23
Phosphorus	mmol/L		0.8	1.6
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150
BUN	mmol/L			2x ULN (mmol/L)
Liver Function				
Test Analyte	**Units**	**Category**	**Clinical Concern Range**	
ALT/SGPT	U/L	High	>=2xULN	
AST/SGOT	U/L	High	>=2xULN	
AlkPhos	U/L	High	>=2xULN	
T Bilirubin	µmol/L	High	>=1.5xULN	

10.8.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec		500
Absolute PR Interval	msec	110	220
Absolute QRS Interval	msec	75	110
Change from Baseline			
Increase from Baseline QTc	msec		>60

10.8.3. Vital Signs

Vital Sign Parameter (Absolute)	Units	Clinical Concern Range	
		Lower	Upper
Systolic Blood Pressure	mmHg	85	160
Diastolic Blood Pressure	mmHg	40	110
Heart Rate	bpm	45	100

Vital Sign Parameter (Change from Baseline)	Units	Clinical Concern Range	
		Increase	
		Lower	Upper
Systolic Blood Pressure	mmHg		>30
Diastolic Blood Pressure	mmHg		>20

10.9. Appendix 9: Abbreviations & Trade Marks

10.9.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
AUC(0-inf)	Area under the concentration-time curve from time zero (predose) extrapolated to infinite time
AUC(0-t)	Area under the concentration-time curve from time zero (predose) to time of last quantifiable concentration within a participant across all treatments
BMI	Body Mass Index
CI	Confidence Interval
Cmax	Maximum observed concentration
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DBF	Database Freeze
DBR	Database Release
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Record Form
EMA	European Medicines Agency
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
GSK	GlaxoSmithKline
IA	Interim Analysis
ICH	International Conference on Harmonization
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
IMMS	International Modules Management System
IP	Investigational Product
ITT	Intent-To-Treat
MMRM	Mixed Model Repeated Measures
NQ	Non-quantifiable
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
PopPK	Population PK
QC	Quality Control

Abbreviation	Description
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RAMOS	Randomization & Medication Ordering System
SAC	Statistical Analysis Complete
SD	Standard deviation
SDSP	Study Data Standardization Plan
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
TA	Therapeutic Area
TFL	Tables, Figures & Listings
tlag	Lab time before observation of drug concentrations in sampled matrix
tlast	Time of last quantifiable concentration
tmax	Time of occurrence of Cmax
WNL	Windows Non Linear

10.9.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
ADVAIR
HARP

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS
WinNonlin 8.1 or above

10.10 Appendix 10: List of Data Displays

10.10.1 Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.11	N/A
Safety	3.1 to 3.23	3.1 to 3.2
Pharmacokinetic	4.1 to 4.4	4.1 to 4.6
Section	**Listings**	
ICH Listings	1 to 26	
Other Listings	27 to 32	

All displays (Tables, Figures & Listings) will use the term 'Subjects'.

10.10.2 Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 11: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	NA	POP_T1	NA
Safety	NA	SAFE_T1	SAFE_L1
Pharmacokinetic	PK_F1	NA	NA

NOTES:

- Non-Standard displays are indicated in the 'IDSL / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

10.10.3 Deliverables

Delivery [Priority] [1]	Description
DR	Dry Run
SAC	Final Statistical Analysis Complete

NOTES:

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

10.10.4 Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Safety	ES1A	Summary of subject Disposition for the subject Conclusion Record	ICH E3, FDAAA, EudraCT	DR , SAC
1.2.	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment	ICH E3	DR , SAC
1.3.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements	DR , SAC
1.4.	Screened	NS1	Summary of Number of subjects by Country and Site ID	EudraCT/Clinical Operations	DR , SAC
Population Analysed					
1.5.	Screened	SP1	Summary of Study Populations	IDSL	DR , SAC
Demographic and Baseline Characteristics					
1.6.	Safety	DM3	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	DR , SAC
1.7.	Randomized	DM11	Summary of Age Ranges	EudraCT	DR , SAC
1.8.	Safety	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT	DR , SAC
Prior and Concomitant Medications					

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.9.	Safety	MH1	Summary of Current/Past Medical Conditions	ICH E3	DR , SAC
Palatability Questionnaire					
1.10	Safety	POP_T1	Responder's Summary of Palatability Questionnaire	Non-standard	DR , SAC
1.11	Safety	SAFE_T1	Responder's compliance to 10 mins for Palatability Questionnaire	Non-standard	DR, SAC

10.10.5 Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	Safety	AE1CP	Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term	ICH E3	DR , SAC
3.2.	Safety	AE1CP	Summary of Treatment Emergent Drug-Related Adverse Events by System Organ Class and Preferred Term/by Overall Frequency	ICH E3	DR , SAC
3.3.	Safety	AE15	Summary of Common (>=2%) Non-serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT	DR , SAC
Serious and Other Significant Adverse Events					

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.4.	Safety	AE16	Summary of Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Number of subjects and Occurrences)	FDAAA, EudraCT	DR , SAC
3.5.	Safety	CP_AE1x	Summary of Treatment Emergent Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term /by Overall Frequency	IDSL	DR , SAC
Laboratory: Chemistry					
3.6.	Safety	LB1	Summary of Chemistry Changes from Baseline	ICH E3	DR , SAC
3.7.	Safety	LB1	Summary of Chemistry Values		DR , SAC
3.8.	Safety	LB17	Summary of Worst Case Chemistry Results by PCI Criteria Post-Baseline Relative to Baseline	ICH E3	DR , SAC
Laboratory: Hematology					
3.9.	Safety	LB1	Summary of Hematology Changes from Baseline	ICH E3	DR , SAC
3.10.	Safety	LB1	Summary of Hematology Values		DR , SAC
3.11.	Safety	LB17	Summary of Worst Case Hematology Results by PCI Criteria Post-Baseline Relative to Baseline	ICH E3	DR , SAC
Laboratory: Urinalysis					
3.12.	Safety	UR1	Summary of Worst-Case Urinalysis Results Post-Baseline Relative to Baseline	ICH E3	DR , SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.13.	Safety	LB1	Summary of Urine Concentration Changes from Baseline	ICH E3 Only where microscopic examination is done	DR , SAC
Laboratory: Hepatobiliary (Liver)					
3.14.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting	IDSL	DR , SAC
3.15.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities	IDSL	DR , SAC
ECG					
3.16.	Safety	EG1	Summary of ECG Findings	IDSL	DR , SAC
3.17.	Safety	EG2	Summary of ECG Values	IDSL	DR , SAC
3.18.	Safety	EG10	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category	IDSL	DR , SAC
3.19.	Safety	CP_EG9	Summary of Change from Baseline in ECG Values by Visit	IDSL	DR , SAC
3.20.	Safety	EG11	Summary of Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category	IDSL	DR , SAC
Vital Signs					
3.21.	Safety	VS1	Summary of Vital Signs	IDSL All vital signs including heart rate and temperature to be summarised.	DR, SAC
3.22.	Safety	VS1	Summary of Change from Baseline in Vital Signs	ICH E3 All vital signs including heart rate and temperature to be summarised.	DR , SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.23.	Safety	VS7	Summary of Worst Case Vital Signs Results by PCI Criteria Post-Baseline Relative to Baseline	IDSL	DR , SAC

10.10.6 Safety Figures

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory					
3.1.	Safety	LIVER14	Scatter Plot of Maximum vs. Baseline for ALT	IDSL	DR , SAC
3.2.	Safety	LIVER9	Scatter Plot of Maximum ALT vs. Maximum Total Bilirubin	IDSL	DR , SAC

10.10.7 Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Plasma GSK1325760					
4.1.	PK	Pkct1	Summary of Plasma GSK1325760 Concentration-Time data by treatment		DR , SAC
4.2.	PK_PAR	Pkpt1	Summary of Untransformed Plasma GSK1325760 Derived Pharmacokinetic Parameters by treatment	Parameters with units	DR , SAC
4.3.	PK_PAR	Pkpt3	Summary of Loge-transformed Plasma GSK1325760 Derived Pharmacokinetic Parameters by treatment	Parameters with units	DR , SAC
PK Statistical Analysis					
4.4.	PK_PAR	PK_T1	Summary of Statistical Analysis of Loge-transformed Plasma GSK1325760 Derived PK Parameters	Footnotes as in example mock shell by treatment	DR , SAC

10.10.8 Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Plasma GSK1325760					
4.1.	PK	Pkcf6	Individual Subject Plasma GSK1325760 Concentration-Time Plots (Linear and Semi-log) by Treatment	Spaghetti plots, all subjects by treatment.	DR, SAC
4.2.	PK	Pkcf1x	Individual Subject GSK1325760 Plasma Concentration-Time Plot (Linear and Semi-log) by Subject	Paginate by Subject. Different point symbol (and colour) to be used for each treatment and to be mentioned in footnote of the figure.	DR, SAC
4.3.	PK	Pkcf4	Arithmetic Mean(+SD) GSK1325760 Concentration-Time Plots (Linear and Semi-log) by Treatment	Different line type (and colour) to be used for each treatment and to be mentioned in footnote of the figure All treatments on one page.	DR, SAC
4.4.	PK	Pkcf5	Median(range) Plasma GSK1325760 Concentration - time Plot (Linear and Semi-log) by Treatment	Different line type (and colour) to be used for each treatment and to be mentioned in footnote of the figure All treatments on one page.	DR, SAC
4.5.	PK_PAR	Pkpf3	Comparative Plot of Individual Subject GSK1325760 Plasma Concentration-Time Derived Parameters vs. Treatment (Linear and semi-logarithmic)	Needed for only AUC(0-inf), AUC(0-t) and Cmax, each parameter on different page. For each parameter all treatments on one page.	DR, SAC
4.6.	PK_PAR	PK_F1	Geometric Mean (90% CI) Treatment Ratios of GSK1325760 Plasma Derived Pharmacokinetic Parameters	Comparison F1-R, F2-R. Needed for only AUC(0-inf), AUC(0-t) and Cmax. [Non-Standard]	DR, SAC

10.10.9 ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Safety	ES3	Listing of Reasons for Study Withdrawal	ICH E3	DR , SAC
2.	Safety	SD3	Listing of Reasons for Study Treatment Discontinuation	ICH E3	DR , SAC
Protocol Deviations					
3.	Safety	DV2A	Listing of Important Protocol Deviations	ICH E3	DR , SAC
4.	Safety	IE4	Listing of subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	DR , SAC
Demographic and Baseline Characteristics					
5.	Safety	DM4	Listing of Demographic Characteristics	ICH E3	DR , SAC
6.	Safety	DM10	Listing of Race	ICH E3	DR , SAC
Prior and Concomitant Medications					
7.	Safety	CM5	Listing of Concomitant Medications	IDSL	DR , SAC
Exposure and Treatment Compliance					
8.	Safety	EX4	Listing of Exposure Data	ICH E3	DR , SAC
Adverse Events					
9.	Safety	AE9CP	Listing of All Adverse Events	ICH E3	DR , SAC
10.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	DR , SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
11.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	DR , SAC
Serious and Other Significant Adverse Events					
12.	Safety	CP_AE9a	Listing of Fatal Serious Adverse Events	ICH E3	DR , SAC
13.	Safety	CP_AE9a	Listing of Non-Fatal Serious Adverse Events	ICH E3	DR , SAC
14.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	DR , SAC
15.	Safety	CP_AE9	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	DR , SAC
All Laboratory					
16.	Safety	CP_LB6	Listing of All Laboratory Data for Subjects with Any Value of Potential Clinical Importance/Outside Normal Range	ICH E3	DR , SAC
17.	Safety	CP_LB6	Listing of Laboratory Values of Potential Clinical Importance		DR , SAC
18.	Safety	LB14	Listing of Laboratory Data with Character Results	ICH E3	DR , SAC
19.	Safety	UR2B	Listing of Urinalysis Data for Subjects with Any Value of Potential Clinical Importance	ICH E3 Abnormal dipstick findings and microscopic results	DR , SAC
ECG					
20.	Safety	CP_EG4	Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance	IDSL	DR, SAC
21.	Safety	CP_EG4	Listing of ECG Values of Potential Clinical Importance	IDSL	DR, SAC
22.	Safety	CP_EG6	Listing of All ECG Findings for Subjects with an Abnormal ECG Finding	IDSL	DR, SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
23.	Safety	CP_EG6	Listing of Abnormal ECG Findings	IDSL	DR, SAC
Vital Signs					
24.	Safety	CP_VS5	Listing of All Vital Signs Data for Subjects with Any Value of Potential Clinical Importance	IDSL	DR, SAC
25.	Safety	CP_VS5	Listing of Vital Signs of Potential Clinical Importance	IDSL	DR, SAC
26.	Safety	CP_VS5	Listing of CFB in Vital Signs of Potential Clinical Importance	IDSL	DR, SAC

10.10.10 Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK					
27.	PK	pkcl1x	Listing of Plasma GSK1325760 Concentration-time Data by treatment	List all the concentration data including unscheduled	DR, SAC
28.	PK_PAR	pkpl1p	Listing of Derived Plasma GSK1325760 Pharmacokinetic Parameters by Treatment		DR, SAC
29.	PK_PAR	Pkpl2	Listing of GSK1325760 Pharmacokinetic Parameter Ratios by treatment		DR, SAC
30.	PK_PAR	NA	RAW SAS Output from Statistical Analysis of GSK1325760 Plasma Pharmacokinetic Parameters		DR, SAC
Study Population					
31.	Safety	SAFE_L1	Listing of all subjects with the time of answering palatability questionnaire	Footnotes	DR, SAC

10.11 Appendix 11: Example Mock Shells for Data Displays

Example: POP_T1
Protocol: 205019
Population: Safety

Table 1.10
Responder's Summary of Palatability Questionnaire

Question No.	Response	Dispersed GSK1325760 (N=20) n(%)
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.		

Note:
Question 1: CCI
Question 2:
Question 3: CCI
Dispersed GSK1325760 : 5 mg (5 x 1 mg tablets) AMB tablet dispersed in water

Example: SAFE_T1
Protocol: 205019
Population: Safety

Table 1.11
Responder's compliance to 10 mins for Palatability Questionnaire

Treatment Period	Dispersed GSK1325760 (N=8) n(%)
Period 1	4(50%)
Period 2	8(100%)
Period 3	8(100%)

Footnote:

Dispersed GSK1325760 : 5 mg (5 x 1 mg tablets) AMB tablet dispersed in water

Example : PK_T1
Protocol : mid205019
Population : PK_PAR

Table 4.4
Summary of Statistical Analysis of Log_e-transformed Plasma GSK1325760 PK Parameters

Parameter	Comparison Test vs Reference	Adjusted Geometric Mean n Test	Adjusted Geometric Mean n Ref	Ratio (Test/Ref)	90% Confidence Interval for the Ratio	%CVw
AUC(0-inf)(units)	Dispersed GSK1325760 vs Marketed AMB	x xx.xx	x xx.xx	x.xxxx	(x.xxxx, x.xxxx)	xx.x
AUC(0-t)(units)	Oral GSK1325760 vs Marketed AMB	x xx.xx	x xx.xx	x.xxxx	(x.xxxx, x.xxxx)	xx.x

FOOTNOTE:
Dispersed GSK1325760: 5mg (5x 1 mg tablets) AMB tablet dispersed in water
Oral GSK1325760: 5mg (5 x 1 mg tablets) AMB tablet administered orally
Marketed AMB: 5 mg (1 x 5 mg tablet) AMB tablet administered orally

Example : SAFE_L1
Protocol : mid205019
Population : Safety

Listing 32

Listing of all subjects with the time of answering palatability questionnaire

Subj.	{Age(y)/ Sex/ Race}	Treatment Period/ Tmt.	Date/Time of Dosing	Date/Time of Questionnaire	Time between dosing and questionnaire (in mins)
PPD	36/ M/ Mixed Race	Period 1/ Dispersed GSK1325760	xx-xx-xx xx:xx:xx	xx-xx-xx xx:xx:xx	Xxx
PPD	33/ M/ Mixed Race	Period 2/ Dispersed GSK1325760	xx.xx	xx-xx-xx xx:xx:xx	Xxx
PPD	24/ M/ Mixed Race	Period 3/ Dispersed GSK1325760	xx.xx	xx-xx-xx xx:xx:xx	xxx

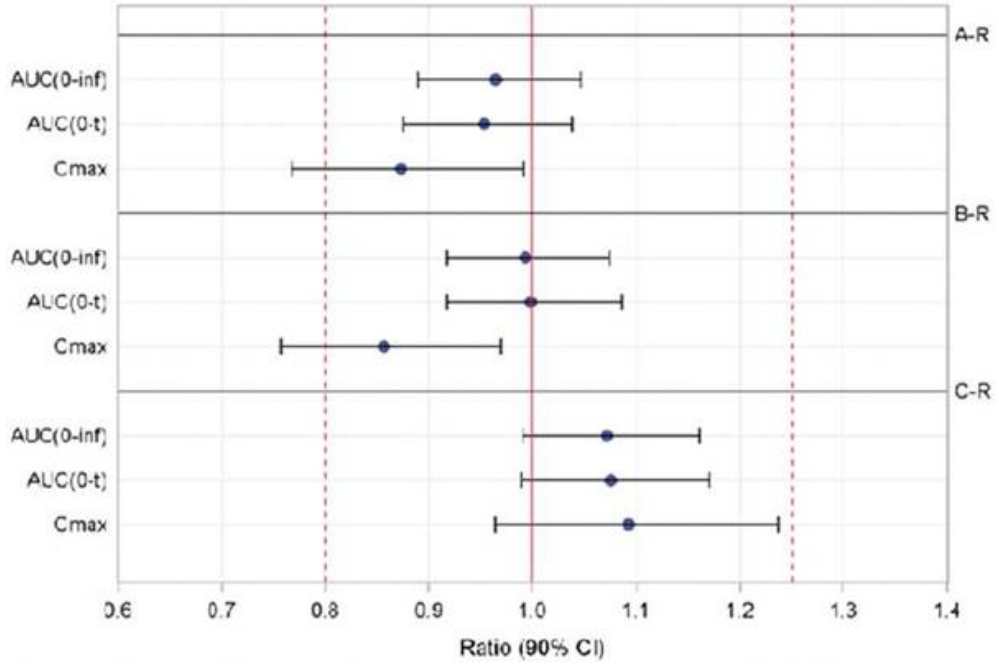
FOOTNOTE:

Dispersed GSK1325760: 5mg (5x 1 mg tablets) AMB tablet dispersed in water

Example : PK_F1
Protocol : mid205019
Population : PK_PAR

Figure 4.6

Geometric Mean Treatment Ratio and 90% CI of Analyte Matrix PK Parameters



Note: A,B,C are test treatments(in this case F1 and F2) and R is the Reference treatment

FOOTNOTE:

Dispersed GSK1325760: 5mg (5x 1 mg tablets) AMB tablet dispersed in water

Oral GSK1325760: 5mg (5 x 1 mg tablets) AMB tablet administered orally

Marketed AMB: 5 mg (1 x 5 mg tablet) AMB tablet administered orally