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

Title	:	Reporting and Analysis Plan for 205037: A single-centre, randomized, double-blind, dose-ascending, placebo-controlled study to evaluate the safety, tolerability, and pharmacokinetics of oral TID doses (one day) of GSK2982772 in Japanese healthy male subjects
Compound Number	:	GSK2982772
Effective Date	:	11-JUL-2018

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 205037.
- This RAP is intended to describe the final analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.

RAP Author(s):

Approver	Date	Approval Method
PPD Biostatistics Group 2, Biomedical Data Sciences Japan	NA	NA

RAP Team Approvals:

Approver	Date	Approval Method
PPD Lead Programmer; Statistical Programming & Reporting Group, Biomedical Data Sciences Japan	10-JUL-2018	Pharma TMF
PPD Clinical Investigation Leader/Operational Science Lead; Clinical Pharmacology Office	09-JUL-2018	Pharma TMF
PPD Data Quality Lead; Data Practice Group, Biomedical Data Sciences Japan	10-JUL-2018	Pharma TMF
PPD PK Analyst; Clinical Pharmacology Office	09-JUL-2018	Pharma TMF

Clinical Statistics and Clinical Programming Line Approvals:

Approver	Date	Approval Method
PPD Lead Authors Line Manager; Biostatistics Group 2, Biomedical Data Sciences Japan	11-JUL-2018	Pharma TMF
PPD Lead Programmers Line Manager; Statistical Programming & Reporting Group, Biomedical Data Sciences Japan	11-JUL-2018	Pharma TMF

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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: 205037

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: 07/JUN/2018).

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

Objectives	Endpoints
• To assess the safety and tolerability of TID doses for one day of GSK2982772 in Japanese healthy male subjects.	• Adverse events (AEs) • Change in laboratory values (clinical chemistry, haematology and urinalysis), 12-lead ECG, vital signs (blood pressure, pulse rate, and body temperature) • Physical examinations, in including neurological examinations.
• To characterise the PK profile of TID doses for one day of GSK2982772 in Japanese healthy male subjects.	• Derived PK parameters for GSK2982772, including area under the plasma drug concentration versus time curve over 24 hr (AUC(0-24)) and AUC over each dose interval (i.e. AUC(0-7), AUC(7-14) and AUC(14-24)). Maximum observed plasma drug concentration (Cmax) following each dose, time to maximum observed plasma drug concentration (Tmax) following each dose, terminal half-life (t1/2) following the third dose, observed trough plasma drug concentrations (C0, C7, C14 and C24), where data allow

2.3. Study Design

Overview of Study Design and Key Features

Group	N	Period 1	Period 2	Period 3	Period 4
A	3	Placebo, TID	60 mg, TID	120 mg, TID	240 mg, TID
B	3	60 mg, TID	Placebo, TID	120 mg, TID	240 mg, TID
C	3	60 mg, TID	120 mg, TID	Placebo, TID	240 mg, TID
D	3	60 mg, TID	120 mg, TID	240 mg, TID	Placebo, TID

Screening	Within 30 days prior to the first dosing.
Treatment Period	The study will be comprised of four study periods each at least 7 days in duration with subjects in-house for 4 nights (through 72 hours after the 1st dose). During each treatment period, subjects will be admitted to the unit the day before dosing and will be discharged after completion of the 72-hour post-dose assessments. Each subject will receive oral TID doses of GSK2982772 in fasted condition in each treatment period. For TID dosing, GSK2982772 or placebo will be administered using a 7 hr, 7 hr dosing interval.
Washout Period	Will be at least 7 days between treatment period doses for an individual subject.
Follow-up	At least 7 days, and no greater than 14 days after last study treatment administration. If warranted, additional follow-up visits may be scheduled.

Design Features	• This study will be a double-blind with respect to subjects, investigator and site staff (with the exception of the unblinded site pharmacist), a three times daily/day, ascending dose, randomized, placebo-controlled, 4-way crossover study.
Dosing	• The initial starting dose planned is 60 mg TID and the maximum dose is 720 mg/day administered as 240 mg TID, which cover the dose range of the proposed Ph2b study. • Sentinel dosing will be employed within each dosing period of the study. The doses in the single-ascending dose portion of the study will be staggered such that for each dose, on Day 1, two of the 12 subjects will be randomized to treatment (one subject will receive GSK2982772 and one subject will receive matched-placebo). Assuming 2 subjects are dosed on Day 1 and assuming adequate safety (AEs, clinical labs, vital signs and ECGs) in the judgment of the principal investigator and GSK Medical Monitor through approximately 24 hours after their 2nd dose on Day 1, the remaining subjects may be randomized to dosing in that period. • 60 mg, 120 mg, and 240 mg of GSK2982772 will be administered in each sentinel dosing which occurred on Period 1, 2, and 3, respectively.
Time & Events	• Refer to Appendix 2: Schedule of Activities
Treatment Assignment	• On Day 1, participants will be assigned a unique number (randomization number) in ascending numerical order. The randomization number encodes the participant's assignment to one of the 4 groups, according to the randomization schedule generated prior to the study by the Biomedical Data Sciences Department at GSK. Each participant will be dispensed blinded study treatment, labelled with his unique randomization number, throughout the study. • Subjects will be randomized to one of four sequences (A, B, C, and D), where the treatments in the sequences are:

Overview of Study Design and Key Features	
	○ A: Placebo TID / 60 mg TID / 120 mg TID / 240 mg TID ○ B: 60 mg TID / Placebo TID / 120 mg TID / 240 mg TID ○ C: 60 mg TID / 120 mg TID / Placebo TID / 240 mg TID ○ D: 60 mg TID / 120 mg TID / 240 mg TID / Placebo TID ○
Interim Analysis	• No interim analysis is planned.

2.4. Statistical Hypotheses / Statistical Analyses

The objectives of this study are to evaluate safety, tolerability and pharmacokinetics of GSK2982772 in healthy Japanese subjects. No formal statistical hypotheses will be tested. Descriptive statistics will be used to assess safety and tolerability. An estimation approach will be used to address the pharmacokinetic study objectives, where point estimates and corresponding confidence intervals will be constructed.

3. PLANNED ANALYSES

3.1. Interim Analyses

A review of safety data will be conducted at the end of each period.

The decision to proceed to higher dose strengths will be made by principal investigator and GSK's Medical Monitor based on assessment of safety and tolerability at the preceding dose. This review can include individual subject data.

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. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed according to RandAll NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All subjects who have a screening visit will be included	• Study Population
Enrolled	• All subjects who passed screening and enter the study will be included. • Note screening failures (who never passed screening even if rescreened) and subjects screened but never enrolled into the study (Reserve, Not Used) are excluded from the Enrolled poputation as they did not enter the study.	• Study Population
Safety	• All subjects who have received at least one dose of study treatment will be included.	• Study Population • Safety
Pharmacokinetic (PK)	• All subjects in the Safety population for whom a pharmacokinetic sample has been obtained and analyzed will be included.	• PK

Refer to Appendix 9: List of Data Displays which details the population used for each display.

4.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, 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.

- Data will be reviewed prior to freezing the database 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 summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
[RandAll NG]		Data Displays for Reporting	
Code	Description	Description	Order in TLF
A1	GSK2982772 60 mg	GSK2982772 60 mg	2
A2	GSK2982772 120 mg	GSK2982772 120 mg	3
A3	GSK2982772 240 mg	GSK2982772 240 mg	4
P	Placebo	Placebo	1

5.2. Baseline Definitions

Baseline definitions are applied to each period.

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

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

5.3. Examination of Covariates, Other Strata and Subgroups

5.3.1. Covariates and Other Strata

The list of covariates may be used in descriptive summaries and statistical analyses. Additional covariates may also be considered.

Category	Details
Covariates	See Section 8.1.5.1, describing pharmacokinetic analyses using statistical model

5.4. 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
9.3	Appendix 3: Study Phases and Treatment Emergent Adverse Events
9.4	Appendix 4: Data Display Standards & Handling Conventions
9.5	Appendix 5: Derived and Transformed Data
9.6	Appendix 6: Reporting Standards for Missing Data
9.7	Appendix 7: Values of Potential Clinical Importance

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the Enrolled or Safety 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 9: List of Data Displays.

Display Type	Data Displays Generated		
	Table	Figure	Listing
Subject Disposition			
Subject Disposition for the Subject Conclusion Record	Y		Y
Screening Status and Reasons for Screen Failure	Y		Y
Number of Subjects Enrolled by Country and Site ID	Y		
Subjects for Whom the Treatment Blind was Broken			Y
Planned and Actual Treatments			Y
Protocol Deviations			
Important Protocol Deviations	Y		Y
Inclusion/Exclusion Criteria Deviations			Y
Population Analysed			
Subjects Excluded from PK Population			Y
Demographic and Baseline Characteristics			
Demographic Characteristics	Y		Y
Race and Racial Combinations	Y		Y
Age Ranges	Y		
Medical Conditions and Concomitant Medications			
Medical Conditions			Y
Concomitant Medications			Y
Exposure and Treatment Compliance			
Exposure to Study Treatment			Y

NOTES:

- Y = Yes display generated.

6.1.1. Details of Planned Study Population Summaries

Subject Disposition

Subject Disposition for the Subject Conclusion Record

The number and percentage of subjects who completed the study as well as subjects who withdrew from the study will be summarized. Reason for withdrawal will also be summarized for subjects who withdrew from the study. Only the total column will appear.

Screening Status and Reasons for Screen Failure

This will be based on Enrolled population. The number and percentage of subjects who passed screening and who failed screening and therefore were not entered into the study will be summarized along with the reasons for failure will be summarized for those subjects who failed screening. Only the total column will appear.

Number of Subjects Enrolled by Country and Site ID

This will be based on Enrolled population. The number of subjects summarized by Country, Site ID and Investigator name will be presented. Only the total column will appear.

Protocol Deviations

Important Protocol Deviations

The number and percentage of subjects who had important protocol deviations defined as part of the protocol deviation management plan for the study, will be summarized. Only the total column will appear.

Demographic and Baseline Characteristics

Demographic Characteristics

The number and percentage of subjects or summary statistics will be provided for each demographic characteristic and only the total column will appear: Sex, Age (years), Age Group (years), Ethnicity, Race detail, Height, Weight, and Body Mass Index. Age Group (years) will be categorized into three ('≤18', '19-64', '≥65'). Each demographic characteristic will be summarized using the minimum set of summary statistics.

Race and Racial Combinations

The five-high level FDA race categories and designated Asian subcategories will be summarized along with all combinations of high level categories which exist in the data. Only the total column will appear.

Age Ranges

The number and percentage of subjects within each age range category will be provided. Only the total column will appear. Age range will be categorized into: 18-64 years, ≥65-84 years. This is based on the standard of EMA clinical trial results disclosure requirements.

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) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 9: List of Data Displays.

Display Type	Absolute		
	Summary		Individual
	T	F	L
Adverse Events (AEs)			
All AEs by SOC and PT	Y		Y
All AEs by Maximum Intensity	Y		
Drug-Related AEs by SOC and PT	Y		
Drug-Related AEs by Maximum Intensity	Y		
Subject Numbers for Individual AEs			Y
Relationship Between AE SOCs, PT and Verbatim Text			Y
Serious and Other Significant AEs			
Serious AEs			Y
AEs Leading to Withdrawal from Study			Y

NOTES:

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

7.1.1. Details of Planned Adverse Events Summaries

Adverse Events (AEs)

All AEs by SOC and PT

The number and percentage of subjects with all relevant adverse events will be summarized by MedDRA System Organ Class and Preferred Term by treatment group. The counting of events and the percentages will be based on the number of subjects on each treatment, so subjects may appear in more than one treatment category.

All AEs by Maximum Intensity by SOC and PT

The number and percentage of subjects with adverse events by intensity (e.g., mild, moderate, severe) will be summarized by MedDRA System Organ Class and Preferred Term by treatment group. The counting of events and the percentages will be based on the number of subjects on each treatment, so subjects may appear in more than one treatment category.

Drug-related AEs by SOC and PT

The number and percentage of subjects with all drug-related adverse events will be summarized by MedDRA System Organ Class and Preferred Term. The counting of events and the percentages will be based on the number of subjects on each treatment, so subjects may appear in more than one treatment category.

Drug-related AEs by Maximum Intensity by SOC and PT

The number and percentage of subjects with drug-related adverse events by intensity (e.g., mild, moderate, severe) will be summarized by MedDRA System Organ Class and Preferred Term. The counting of events and the percentages will be based on the number of subjects on each treatment, so subjects may appear in more than one treatment category.

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 9: List of Data Displays.

Display Type	Absolute		
	Summary		Individual
	T	F	L
Chemistry			
Chemistry Changes from Baseline	Y		
Chemistry Values	Y		Y
Chemistry Data Shifts from Baseline Relative to Normal Range	Y		
All Chemistry Data for Subjects with any Value of PCI			Y
Chemistry Values of PCI			Y
Haematology			
Haematology Changes from Baseline	Y		
Haematology Values	Y		Y
Haematology Data Shifts from Baseline Relative to PCI Criteria	Y		
All Haematology Data for Subjects with any Value of PCI			Y
Haematology Values of PCI			Y
Urinalysis			
Urinalysis Concentration Changes from Baseline (Gravity and pH)	Y		
Urinalysis Data (Gravity and pH)	Y		Y
Urinalysis Data (Glucose, Protein, Blood, Ketones, Bilirubin, and Urobilinogen)	Y		Y
Hepatobiliary (Liver)			
Liver Monitoring/Stopping Event Reporting			Y
Medical Conditions for Subjects with Liver Stopping Events			Y

NOTES:

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

7.2.1. Details of Planned Clinical Laboratory Displays

Chemistry/Haematology Laboratory Tests

Laboratory Changes from Baseline and Values

Each quantitative laboratory test and the changes in value from baseline will be summarized at every assessed time point using n, mean, standard deviation, median, minimum, and maximum by treatment group.

Laboratory Data Shifts from Baseline Relative to PCI Criteria

The number and percentage of subjects with laboratory results within each PCI criteria category (Low, W/in Range, High) during each planned time assessment will be summarized by treatment group relative to their baseline category by laboratory test, where PCI criteria are available. The percentages are based on the number of subjects in the treatment group with data for the laboratory test at the specified planned time (n). The worst case post-baseline is used to summarize the subjects' overall worst case shifts during the post-baseline period.

Urinalysis Laboratory Tests

Urinalysis Concentration Changes from Baseline (Gravity and pH)

Gravity and pH test and the changes in value from baseline will be summarized at every assessed time point using n, mean, standard deviation, median, minimum, and maximum by treatment group.

Urinalysis Data (Glucose, Protein, Blood, Ketones, Bilirubin, and Urobilinogen)

The number and percentage of subjects with the above urinalysis results (character results) will be summarized by treatment group.

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 9: List of Data Displays.

Display Type	Absolute			Change from BL		
	Summary		Individual	Summary		Individual
	T	F	L	T	F	L
Neurological Examination						
Neurological Examination Findings	Y		Y			
ECG						
ECG Findings	Y		Y			
ECG Values	Y		Y	Y		
All ECG Values for Subjects with any Value of PCI			Y			
Cardiac Telemetry	Y					
Cardiac Telemetry Abnormalities	Y					
Clinically Significant Cardiac Telemetry Abnormalities			Y			
Vital Signs						
Vitals Values	Y		Y	Y		
All Vital Signs for Subjects with any Value of PCI			Y			

NOTES:

- T = Table, F = Figures, L = Listings, Y = Yes display generated, PCI = Potential Clinical Importance
- 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.

7.3.1. Details of Planned Other Safety Displays

ECG

ECG Findings

The number and percentage of subjects with ECG findings (ECG interpretation) will be summarized by treatment group..

ECG Values

Each ECG parameter value and the change from baseline will be summarized by treatment group at every assessed time point using n, mean, standard deviation, median, minimum, and maximum.

Cardiac Telemetry

The number and percentage of subjects with telemetry result of "normal," "abnormal but clinically insignificant," and "abnormal and clinically significant" will be summarized by

treatment group. The number and percentage of subjects with specific telemetry abnormalities will be summarized by treatment group.

Vital Signs

Vital Signs

Each vital sign parameter and the changes in value from baseline will be summarized by treatment group at every assessed time point using n, mean, standard deviation, median, minimum, and maximum.

8. PHARMACOKINETIC ANALYSES

8.1. Pharmacokinetic Analyses

8.1.1. Endpoint / Variables

8.1.1.1. Drug Concentration Measures

Refer to Appendix 4: Data Display Standards & Handling Conventions (Section 9.4.3 Reporting Standards for Pharmacokinetic)

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 6.3 or hihger. All calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters listed will be determined from the plasma concentration-time data, as data permits.

Parameter	Parameter Description
AUC(0-7), AUC(7-14), AUC(14-24), AUC(0-24)	The area under the concentration-time curve will be calculated to some fixed nominal time x (AUC(0-x), using the combination of linear and logarithmic trapezoidal methods (i.e., Linear Up/Log Down calculation method in Phoenix WinNonlin Professional). If a sampling time deviation occurred at nominal time x (and x < t), AUC(0-x) will be calculated using the concentration at time x post-dose estimated by the method of interpolation. If nominal time x > t (or if the concentration at time x was below the limit of quantification), then the concentration (y) at time x is estimated using lambda_z and last observed Ct according to the formula: $y = Ct(obser) \times e^{-lambda\_z(x-t)}$ Then the following equation will be used to calculate (AUC(0-x)) where t is the time of last quantifiable plasma concentration. AUC(0-x) = AUC(0-t) x AUC(t-x) If lambda_z is not estimable, a partial AUC is not calculated (when x > t).
Cmax	Maximum observed plasma concentration following each dose will be obtained directly from the concentration-time data.
Tmax	The time to maximum observed plasma drug concentration following each dose will be obtained directly from the concentration-time data.
t1/2	Terminal half-life following the 3rd dose will be calculated as follows: t1/2 = ln2 / lambda_z
C0	The plasma drug concentration at 0 hour will be obtained directly from the observed concentration-time data.
C7	The plasma drug concentration at 7 hours will be obtained directly from the observed concentration-time data.
C14	The plasma drug concentration at 14 hours will be obtained directly from the observed concentration-time data.
C24	The plasma drug concentration at 24 hours will be obtained directly from the observed concentration-time data.

Parameter	Parameter Description
lambda_z	The first order rate constant associated with the terminal (log-linear) portion of the curve following the 3rd dose.
lambda_z lower	The lower limit on time for values to be included in the calculation of lambda_z following the 3rd dose..
lambda_z upper	The upper limit on time for values to be included in the calculation of lambda_z following the 3rd dose..
#pts	The number of time points used in computing lambda_z following the 3rd dose..
R-square	Square of the correlation coefficient for computing lambda_z following the 3rd dose.

NOTES:

- Additional parameters may be included as required.
- Lambda_z is the terminal phase rate constant.
- Ct is the last observed quantifiable concentration.

8.1.2. Summary Measure

The slope of log-transformed dose in the power model for AUC(0-24), AUC(0-7) and Cmax will be used as measure of the dose proportionality between dose and the PK parameters..

8.1.3. Population of Interest

The primary pharmacokinetic analyses will be based on the Pharmacokinetic population, unless otherwise specified.

8.1.4. Strategy for Intercurrent (Post-Randomization) Events

Intercurrent events which may affect the assessment of the safety and tolerability and the characterization of PK profile will not be anticipated.

8.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 9: 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 participants have well defined plasma profiles).

Endpoint / Variables
• Derived PK parameters for GSK2982772 (AUC(0-24), AUC(0-7), Cmax)

Model Specification

- Dose proportionality for AUC(0-24), AUC(0-7) and Cmax following the first (morning) dose will be assessed by using a power model as described below:

$$\log_e (Y_{ij}) = \mu + S_i + \beta * \log_e (D_j) + \varepsilon_{ij}$$

Y_{ij}: PK parameter (AUC(0-24), AUC(0-7), Cmax) on dose j for subject i

μ: Overall mean (intercept)

β: slope for $\log_e$ transformed dose

S_i: random effect for subject i following normal distribution $N(0, \sigma_b^2)$

D_j: dose effect (j= 60 mg, 120 mg, 240 mg)

ε_{ij}: random error following normal distribution $N(0, \sigma_w^2)$

- The model parameters will be estimated using Restricted Maximum Likelihood with the Newton-Raphson algorithm.
- The Kenward-Roger degree of freedom approach will be used.

Model Checking & Diagnostics

- If the power model has failed to converge, dose proportionality will be assessed using ANOVA.
  - Assessment of dose proportionality using ANOVA
    - The dose-normalized PK parameters (AUC(0-24), AUC(0-7), Cmax) will be calculated by dividing the PK parameters by dose.
    - The dose-normalized values will be analyzed by using the following model.

$$\log (X_{ij}) = \mu + S_i + D_j + \varepsilon_{ij}$$

X_{ij} : dose-normalized PK parameter (AUC(0-24), AUC(0-7), Cmax) on the dose j for subject i

μ : Overall mean

S_i: random effect for subject i following normal distribution $N(0, \sigma_b^2)$

D_j : dose effect (j= 60 mg, 120 mg, 240 mg)

ε_{ij} : random error following normal distribution $N(0, \sigma_w^2)$

the model has dose as fixed effect and subject as random effect.

    - Point estimates and associated 90% confidence intervals for the differences 60 mg – 120 mg, 240 mg – 120 mg will be construced using the residual variance. These confidence intervals will then be exponentially back-transformed to provide point estimates and associated 90% confidence intervals for the ratio 60 mg/120 mg and 240 mg/120 mg.

Model Results Presentation

- The point estimates of the slope for each parameter and their 90% confidence intervals will be presented.

8.1.6. Details of Planned Pharmacokinetic Displays

Plasma Concentration-Time Data

The plasma concentrations at every scheduled time point will be summarized using n, mean, standard deviation, median, minimum, and maximum.

Derived Plasma Pharmacokinetic Parameters (non-transformed)

The plasma pharmacokinetic parameters (AUC(0-7), AUC(7-14), AUC(14-24), AUC(0-24), Cmax, Tmax, t1/2, C0, C7, C14, C24) will be summarized using n, mean, 95% CI, standard deviation, median, minimum, and maximum.

Derived Plasma Pharmacokinetic Parameters (log-transformed)

For each pharmacokinetic parameters with a log-normal distribution (AUC(0-7), AUC(7-14), AUC(14-24), AUC(0-24), Cmax, t1/2, C0, C7, C14, C24), the log-transformed parameters will be summarized using n, geometric mean, 95% CI of geometric mean, standard deviation of log-transformed data and between subject coefficient of variation (%CVb).

Power Model Analysis for Dose Proportionality of Pharmacokinetic Parameters AUC(0-24), AUC(0-7) and Cmax

The analysis results will be presented as described in Section 8.1.5.1.

9. APPENDICES

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

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the PDMP and the data handling will be determined prior to DBR.

9.2. Appendix 2: Schedule of Activities

9.2.1. Protocol Defined Schedule of Events

Time and Events Table for Screening and Follow-up Assessments

Procedure	**Screening[1]**	**Follow-up Visit[2]**	***Notes***
Outpatient Visit	X	X	
Informed Consent	X		
Medical/medication/drug /alcohol history	X		
Demographics	X		
Physical Examination	X	X	*Additional examinations may be performed, by the Investigators, as deemed necessary (e.g., where safety or laboratory findings indicate).*
Drug screen	X		*Additional tests may be performed by the Investigators, as deemed necessary (e.g., where safety or laboratory findings indicate). Tests will be conducted within site specified standards.*
Syphilis, Human immunodeficiency virus (HIV), Human T-cell leulemia virus type 1 (HTLV-1), Hepatitis B (Hep B) and Hepatitis C (Hep C) screen	X		
Tuberculosis (TB) Test	X		Conducted at the standard practice of the site.
X-ray Test	X		Anterior & lateral chest X-ray will be taken.
Hema/Chem/Urinalysis tests	X	X	
Height and weight	X		
12-lead ECG and vital signs	X	X	*Vital signs to include pulse rate (PR), blood pressure (BPs) and temperature.*
AE Review	X	X	*All Serious Adverse Effects (SAEs) will be collected from the signing of the informed consent form (ICF) until the follow-up visit at the time points specified. All AEs will be collected from the start of treatment until the follow-up visit at the time points specified.*
Concomitant Medication Review	X	X	

1: Within 30 days prior to the first dosing

2: Follow-up Visit to occur at least 7 days, and no greater than 14 days after last study treatment administration. If a participant withdrew from the study after received GSK2982772 or placebo dose, the safety assessments listed at follow-up visit will be required.

Detailed Time and Events Table for Days 1-4 (common Period1-4)

Procedure [1]	Day -1	Day 1																						
		Pre-dose	0	20 min	40 min	1 hr	1.5 hr	2 hr	3 hr	4 hr	5 hr	7 hr	7 hr 20 min	7 hr 40 min	8 hr	8.5 hr	9 hr	10 hr	12 hr	14 hr	14 hr 20 min	14 hr 40 min	15 hr	15.5 hr
Admission	X																							
Physical Examination	X	X																	X[6]					
Hema/Chem/ Urinalysis tests	X																							
Vital signs [2]		X						X											X	X				
12-lead ECG		X						X											X[5]	X				
Cardiac telemetry		<==========																						
PK blood sampling		X		X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Neurological Examination	X							X												X				
Study Treatment			X									X								X				
Pharmacogenetic Sample (PGx) [3]		<==========																						
Meals Served	X									X[6]								X[7]						
AE Review [4]	<==========																							
Concomitant Medication Review	<==========																							
Discharge																								

Procedure [1]	Day 2								Day 3		Day 4
	16 hr	17 hr	19 hr	22 hr	24 hr	28 hr	32 hr	36 hr	48 hr	60 hr	72 hr
Admission											
Physical Examination					X			X	X		X
Hema/Chem/ Urinalysis tests											X
Vital signs [2]					X				X		X
12-lead ECG					X				X		X
Cardiac telemetry	==========>										
PK blood sampling	X	X	X	X	X	X	X	X	X	X	X
Neurological Examination					X				X		X
Study Treatment											
Pharmacogenetic Sample (PGx) [3]	==========>										
Meals Served					X[8]	X[8]	X[8]		X[8]	X[8]	
AE Review [4]	==========>										
Concomitant Medication Review	==========>										
Discharge											X

1: In this study, baseline is Day -1 and Day 1 pre-dose tests.
2: Vital signs include PR, BPs and temperature. A 14 hr time point is to be performed prior to third dose.
3: A PGx blood sample will be collected at any time during the study after randomization. The participation is optional for each subject.
4: All SAEs will be collected from the signing of the ICF until the follow-up visit at the time points specified. All AEs will be collected from the start of treatment until the follow-up visit at the time points specified.
5: Physical Examination and 12-lead ECG of 14hr time point are to be performed prior to third dose.
6: On Day 1, lunch will be served between 2 to 3 hr prior second dose.
7: On Day1, dinner will be served between 2 to 3 hr prior to third dose.
8: On Day 2-3, meal will be served per unit schedule. Mealtime will be described in SRM.

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

9.3.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to the date of dosing date.

Study Phase	Definition
Pre-Treatment	Date ≤ Previous Day of Dosing Date in Period 1
Period 1	Previous Day of Dosing Date in Period 1 ≤ Date < Previous Day of Dosing Date in Period 2
Period 2	Previous Day of Dosing Date in Period 2 ≤ Date < Previous Day of Dosing Date in Period 3
Period 3	Previous Day of Dosing Date in Period 3 ≤ Date < Previous Day of Dosing Date in Period 4
Period 4	Previous Day of Dosing Date in Period 4 ≤ Date

9.3.1.1. Study Phases for Adverse Events

Study Phase	Definition
Pre-Treatment	AE Onset Date and Time < Study First Dosing Date and Time
Period 1	Dosing Date and Time in Period 1 ≤ AE Onset Date and Time < Dosing Date and Time in Period 2
Period 2	Dosing Date and Time in Period 2 ≤ AE Onset Date and Time < Dosing Date and Time in Period 3
Period 3	Dosing Date and Time in Period 3≤ AE Onset Date and Time < Dosing Date and Time in Period 4
Period 4	Dosing Date and Time in Period 4≤ AE Onset Date and Time
Time since Study First Dose (min)	If study phase of the event is pre-treatment, AE Onset Date and Time - Study First Dosing Date and Time 1 otherwise AE Onset Date and Time – Study First Dosing Date and Time + 1 min
Time since Period First Dose (min)	If study phase of the AE is pre-treatment, set to missing If study phase of the AE is period 1, AE Onset Date and Time – Dosing Date and Time in Period 1 + 1 min If study phase of the AE is period 2, AE Onset Date and Time – Dosing Date and Time in Period 2 + 1 min If study phase of the AE is period 3, AE Onset Date and Time – Dosing Date and Time in Period 3 + 1 min If study phase of the AE is period 4, AE Onset Date and Time – Dosing Date and Time in Period 4 + 1 min
Time since Last Dose (min)	If study phase of the AE is pre-treatment, set to missing If study phase of the AE ≥ Study Last Dosing Start Date and Time, AE Onset Date and Time – Study Last Dosing Start Date and Time+ 1 min
Duration (min)	AE Resolution Date and Time – AE Onset Date and Time + 1 min
Drug-related	If relationship is marked 'YES' on eCRF or value is missing.

NOTES:

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

9.3.1.2. Study Phases for Concomitant Medication

The study phase for concomitant medication will be categorized into pre-treatment, period 1, period 2, period 3, and period 4 based on medication start date and time.

Study Phase	Definition
Pre-Treatment	Start Date and Time < Dosing Date in Period 1
Period 1	Dosing Date in Period 1 ≤ Start Date and Time < Dosing Date in Period 2
Period 2	Dosing Date in Period 2 ≤ Start Date and Time < Dosing Date in Period 3
Period 3	Dosing Date in Period 3 ≤ Start Date and Time < Dosing Date in Period 4
Period 4	Dosing Date in Period 4 ≤ Start Date and Time

NOTES:

- Please refer to Appendix 6: Reporting Standards for Missing Data for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

9.4. Appendix 4: Data Display Standards & Handling Conventions

9.4.1. Reporting Process

Software	
• The currently supported versions of SAS software [Insert Other Software as Required] will be used.	
Reporting Area	
HARP Server	: N/A
HARP Compound	: N/A
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.0.	
Generation of RTF Files	
• RTF files will be generated.	

9.4.2. 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
• Do not include subject level listings in the main body of the GSK Clinical Study Report. All subject level listings should be located in the modular appendices as ICH or non-ICH listings

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.
  • For [Insert Endpoint / Parameter] the following DP's places will be applied:
  • Summary Statistics:
  • Listings:

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. • [Insert as Required: If any publication related displays have been specified, please provide relevant details]	

9.4.3. Reporting Standards for Pharmacokinetic

Pharmacokinetic Concentration Data	
PC Windows Non-Linear (WNL) File	PC WNL file (CSV format) for the non compartmental analysis by Clinical Pharmacology Office function will be created according to GUI_51487. Note: Concentration values will be imputed as per GUI_51487
Descriptive Summary Statistics, Graphical Displays and Listings	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.
Pharmacokinetic Parameter Derivation	
PK Parameter to be Derived by Programmer	The following PK parameters will be derived by the Programmer: [C0, C7, C14, C24]
Pharmacokinetic Parameter Data	
Is NQ impacted PK Parameters Rule Being Followed	Yes, refer to GUI_51487.
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Refer to [Insert document name]

9.5. Appendix 5: Derived and Transformed Data

9.5.1. 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

Period Day

• Calculated as the number of days from Dosing Date in each period. For study phase derivation, see Appendix 3.
  • If Study Phase of Ref Assessment or Event = Pre-Treatment or Missing
  → Period Day = Missing
  • If Study Phase of Ref Assessment or Event = Period X and Ref Date is on or after Dosing Date in Period X
  → Period Day = Ref Date – Dosing Date in Period X + 1 day
  • If Study Phase of Ref Assessment or Event = Period X and Ref Date is before Dosing Date in Period X
  → Period Day = Ref Date – Dosing Date in Period X
  Note: X takes a value of 1, 2, 3, 4.

9.5.2. Study Population

Age
• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows: ○ A date and month will be imputed as '30th June' as it will not be captured. • Date of Informed Consent will be used as reference date of calculation.

9.5.3. Safety

Laboratory Parameters
Imputation
• 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. o Example 1: 2 Significant Digits = '< x' becomes x – 0.01 o Example 2: 1 Significant Digit = '> x' becomes x + 0.1 o Example 3: 0 Significant Digits = '< x' becomes x – 1 • The default convention for reporting of clinical laboratory units will be the international system of units (SI units).

9.6. Appendix 6: Reporting Standards for Missing Data

9.6.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as completion of all phases of the study including the last visit or the last scheduled procedure. • Withdrawn subjects may 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 slotted as per Appendix 3: Assessment Windows or will be summarised as withdrawal visits.

9.6.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: ○ These data will be indicated by the use of a “blank” in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. ○ Answers such as “Not applicable” and “Not evaluable” are not considered to be missing data and should be displayed as such.
Outliers	• Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

9.6.2.1. 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. • The eCRF allows for the possibility of missing times to be recorded for AE start and end dates. Missing dates will be imputed using the following convention: ○ If the missing time is a start date, a '00:00' will be used for the time. ○ If the missing date is a stop date, a '23:59' will be used for the time. • The recorded missing time will be displayed in listings without imputed values.
Concomitant Medications/ Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month ○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The eCRF allows for the possibility of missing times to be recorded for concomitant medications start and end dates. Missing dates will be imputed using the following convention: ○ If the missing time is a start date, a '00:00' will be used for the time.

Element	Reporting Detail
	○ If the missing date is a stop date, a '23:59' will be used for the time. • The recorded partial date and missing time will be displayed in listings without imputed values.

9.7. Appendix 7: Values of Potential Clinical Importance

9.7.1. Laboratory Values

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Hematocrit	Ratio of 1			0.54
		Δ from BL	↓ 0.075	
Haemoglobin	g/L			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
White 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	mmol/L		3	9
Phosphorus	mmol/L		0.8	1.6
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150

Liver Function			
Test Analyte	**Units**	**Category**	**Clinical Concern Range**
ALT/SGPT	U/L	High	≥ 2x ULN
AST/SGOT	U/L	High	≥ 2x ULN
AlkPhos	U/L	High	≥ 2x ULN
T Bilirubin	µmol/L	High	≥ 1.5xULN
T. Bilirubin + ALT	µmol/L U/L	High	1.5xULN T. Bilirubin + ≥ 2x ULN ALT

9.7.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec		> 450 [1]
Absolute PR Interval	msec	< 110 [1]	> 220 [1]
Absolute QRS Interval	msec	< 75 [1]	> 110 [1]
Change from Baseline			
Increase from Baseline QTc	msec		> 60 [1]

NOTES:
1. Represent standard ECG values of PCI for HV studies

9.7.3. Vital Signs

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

9.8. Appendix 8: Abbreviations & Trade Marks

9.8.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
A&R	Analysis and Reporting
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DBF	Database Freeze
DBR	Database Release
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
ICH	International Conference on Harmonization
IDSL	Integrated Data Standards Library
ITT	Intent-To-Treat
PCI	Potential Clinical Importance
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
RAP	Reporting & Analysis Plan
SAC	Statistical Analysis Complete
SDSP	Study Data Standardization Plan
SDTM	Study Data Tabulation Model
TFL	Tables, Figures & Listings

9.8.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS
WinNonlin

9.9. Appendix 9: List of Data Displays

9.9.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.7	-
Safety	2.1 to 2.21	-
Pharmacokinetic	3.1 to 3.5	3.1 to 3.5
Section	**Listings**	
ICH Listings	1 to 37	

9.9.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 10: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Safety	SAF_Fn	SAF_Tn	SAF_Ln

NOTES:

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

9.9.3. Deliverables

Delivery	Description
SAC	Final Statistical Analysis Complete

9.9.4. 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 Participant Conclusion Record	ICH E3, FDAAA, EudraCT	SAC
1.2.	Enrolled	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements	SAC
1.3.	Enrolled	NS1	Summary of Number of Participant by Country and Site ID	EudraCT/Clinical Operations	SAC
Protocol Deviation					
1.4.	Safety	DV1	Summary of Important Protocol Deviations	ICH E3	SAC
Demographic and Baseline Characteristics					
1.5.	Safety	DM3	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	SAC
1.6.	Safety	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT	SAC
1.7.	Enrolled	DM11	Summary of Age Ranges	EudraCT	SAC

9.9.5. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
2.1.	Safety	AE1CP	Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3	SAC
2.2.	Safety	AE5A	Summary of All Adverse Events by Maximum Intensity by System Organ Class and Preferred Term	ICH E3	SAC
2.3.	Safety	AE1CP	Summary All Drug-Related Adverse Events by System Organ Class and Preferred Term	ICH E3 .	SAC
2.4.	Safety	AE5A	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term and Maximum Intensity	ICH E3 .	SAC
Laboratory: Chemistry					
2.5.	Safety	LB1	Summary of Chemistry Values		SAC
2.6.	Safety	LB1	Summary of Chemistry Changes from Baseline	ICH E3	SAC
2.7.	Safety	LB4	Summary of Chemistry Data Shifts from Baseline Relative to PCI Criteria	ICH E3	SAC
Laboratory: Hematology					
2.8.	Safety	LB1	Summary of Hematology Values		SAC
2.9.	Safety	LB1	Summary of Hematology Changes from Baseline	ICH E3	SAC
2.10.	Safety	LB4	Summary of Hematology Data Shifts from Baseline Relative to PCI Criteria	ICH E3	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Urinalysis					
2.11.	Safety	LB1	Summary of Urinalysis Data (Gravity and pH)		SAC
2.12.	Safety	LB1	Summary of Urinalysis Concentration Change from Baseline (Gravity and pH)	ICH E3	SAC
2.13.	Safety	UR3b	Summary of Urinalysis Data (Glucose, Protein, Blood, Ketones, Bilirubin, Urobilinogen)		SAC
Neurological Examination					
2.14.	Safety	NE1	Summary of Neurological Examination		SAC
ECG					
2.15.	Safety	EG1	Summary of ECG Findings	IDSL	SAC
2.16.	Safety	EG2	Summary of ECG Values		SAC
2.17.	Safety	EG2	Summary of Change from Baseline in ECG Values by Visit	IDSL	SAC
2.18.	Safety	HM1	Summary of Cardiac Telemetry	IDSL	SAC
2.19.	Safety	HM2	Summary of Cardiac Telemetry Abnpormalities	IDSL	SAC
Vital Signs					
2.20.	Safety	VS1	Summary of Vital Signs	IDSL	SAC
2.21.	Safety	VS1	Summary of Change from Baseline in Vital Signs	ICH E3	SAC

9.9.6. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.1.	PK	PK01	Summary of GSK2982772 Plasma Pharmacokinetic Concentration-Time Data		SAC
3.2.	PK	PK03	Summary of Derived GSK2982772 Pharmacokinetic Parameters (non-transformed)		SAC
3.3.	PK	PK05	Summary of GSK2982772 Pharmacokinetic Parameters (log-transformed)		SAC
3.4.	PK	PK_T1	Power Model Analysis for GSK2982772 Dose Proportionality of Pharmacokinetic Parameters (AUC(0-24), AUC(0-7), Cmax)		SAC
3.5.	PK	PK_T2	ANOVA Model Analysis for GSK2982772 Dose Proportionality of Dose-Normalized Derived Pharmacokinetic Parameters(AUC(0-24), AUC(0-7), Cmax)	This table will be provided if the power model fails to converge.	SAC

9.9.7. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.1.	PK	PK16b	Individual GSK2982772 Plasma Concentration–Time Plots by Subject	A graph on linear and semi-logarithmic scales will be produced.	SAC
3.2.	PK	PK24	Individual GSK2982772 Plasma Concentration–Time Plots by Treatment	A graph on linear and semi-logarithmic scales will be produced.	SAC
3.3.	PK	PK17	Mean (+SD) GSK2982772 Plasma Concentration–Time Plots	A graph on linear and semi-logarithmic scales will be produced. SD will also be displayed.	SAC
3.4.	PK	PK18	Median GSK2982772 Plasma Concentration–Time Plots	A graph on linear and semi-logarithmic scales will be produced.	SAC
3.5.	PK	PK28	Plot of Individual (+Geometric Mean and 95% CIs) GSK2982772 Pharmacokinetic Parameters (AUC(0-24), AUC(0-7), Cmax) versus Dose		SAC

9.9.8. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Screened	ES7	Listing of Reasons for Screen Failure	Journal Guidelines	SAC
2.	Safety	ES3	Listing of Reasons for Study Withdrawal	ICH E3	SAC
3.	Safety	SD3	Listing of Reasons for Study Treatment Discontinuation	ICH E3	SAC
4.	Safety	BL2	Listing of Participants for Whom the Treatment Blind was Broken	ICH E3	SAC
5.	Safety	TA2	Listing of Planned and Actual Treatments	IDSL	SAC
Protocol Deviations					
6.	Safety	DV2	Listing of Important Protocol Deviations	ICH E3	SAC
7.	Safety	IE4	Listing of Participants with Inclusion/Exclusion Criteria Deviations	ICH E3	SAC
Populations Analysed					
8.	Safety	SP3A	Listing of Subjects Excluded from Any Population	ICH E3	SAC
Demographic and Baseline Characteristics					
9.	Safety	DM4	Listing of Demographic Characteristics	ICH E3	SAC
10.	Safety	DM10	Listing of Race	ICH E3	SAC
Prior and Concomitant Medications					
11.	Safety	MH3	Listing of Medical Conditions	IDSL	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
12.	Safety	CM5	Listing of Concomitant Medications	IDSL	SAC
Exposure and Treatment Compliance					
13.	Safety	EX4	Listing of Exposure Data	ICH E3	SAC
Adverse Events					
14.	Safety	AE9CP	Listing of All Adverse Events	ICH E3	SAC
15.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	SAC
16.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	SAC
Serious and Other Significant Adverse Events					
17.	Safety	AE9CP	Listing of Fatal Serious Adverse Events	ICH E3	SAC
18.	Safety	AE9CP	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	SAC
Hepatobiliary (Liver)					
19.	Safety	MH2	Listing of Medical Conditions for Participants with Liver Stopping Events	IDSL	SAC
20.	Safety	SU2	Listing of Substance Use for Participants with Liver Stopping Events	IDSL	SAC
Chemistry					
21.	Safety	LB6	Listing of All Chemistry Data	ICH E3	SAC
22.	Safety	LB6	Listing of All Chemistry Data for Subjects with Any Value of Potential Clinical Importance	ICH E3	SAC
23.	Safety	LB6	Listing of Chemistry Values of Potential Clinical Importance		SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Haematology					
24.	Safety	LB6	Listing of All Haematology Data	ICH E3	SAC
25.	Safety	LB6	Listing of All Haematology Data for Subjects with Any Value of Potential Clinical Importance	ICH E3	SAC
26.	Safety	LB6	Listing of Haematology Values of Potential Clinical Importance		SAC
Urinarysis					
27.	Safety	LB6	Listing of Urinarysis Data (Gravity and pH)		SAC
28.	Safety	LB14	Listing of Urinarysis Data (Glucose, Protein, Blood, Ketones, Bilirubin, and Urobilinogen)		SAC
Neurological Examination					
29.	Safety	NE2	Listing of Neurological Examinations	IDSL	SAC
ECG					
30.	Safety	EG6	Listing of ECG Findings		SAC
31.	Safety	EG4	Listing of All ECG Values	IDSL	SAC
32.	Safety	EG4	Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance	IDSL	SAC
33.	Safety	HM10	Listing of Clinically Significant Cardiac Telemetry Abnormalities	IDSL	SAC
Vital Signs					
34.	Safety	VS5	Listing of All Vital Signs Data	IDSL	SAC
35.	Safety	VS5	Listing of All Vital Signs Data for Subjects with Any Value of Potential Clinical Importance	IDSL	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetics					
36.	PK	PK08	Listing of GSK2982772 Plasma Pharmacokinetic Concentration-Time Data	IDSL	SAC
37.	PK	PK14	Listing of Derived GSK2982772 Plasma Pharmacokinetic Parameters	IDSL All PK parameters in Section 8.1.1.2 will be provided in a listing	SAC

9.10. Appendix 10: Example Mock Shells for Data Displays

Example: PK_T1
Protocol: 205037 Page 1 of 1
Population: PK

Table x.x
Power Model Analysis for GSK2982772 Dose Proportionality of Pharmacokinetic Parameters (AUC(0-24), AUC(0-7), Cmax)

Parameter	Effect	n	Slope Point Estimate	90% CI
AUC(0-24)	Log(dose levels)	xx	xxx	(xx,xx)
AUC(0-7)	Log(dose levels)	xx	xxx	(xx,xx)
Cmax	Log(dose levels)	xx	xxx	(xx,xx)

Note: The power model was fitted to loge-transformed PK parameters with loge-transformed dose as fixed effet. The slope with corresponding 90% confidence interval was estimated from the power model to assess the degree of dose-proportionality (slope around unity indicates dose-proportionality).

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Example: PK_T2
Protocol: 205037
Population: PK

Table x.x
ANOVA Model Analysis for GSK2982772 Dose Proportionality of Dose-Normalized Derived Pharmacokinetic Parameters(AUC(0-24), AUC(0-7), Cmax)

Parameter	Treatment Comparison	Ratio of Adjusted Geo. Means	90% CI
AUC(0-24)	60 mg / 120 mg	x.xxx	(x.xxx,x.xxx)
	240 mg / 120 mg	x.xxx	(x.xxx,x.xxx)
AUC(0-7)	60 mg / 120 mg	x.xxx	(x.xxx,x.xxx)
	240 mg / 120 mg	x.xxx	(x.xxx,x.xxx)
Cmax	60 mg / 120 mg	x.xxx	(x.xxx,x.xxx)
	240 mg / 120 mg	x.xxx	(x.xxx,x.xxx)

Note: The ANOVA model was fitted to loge-transformed and dose-normalized PK parameters with dose as fixed effet. The ratios of adjusted geographic means with corresponding 90% confidence interval were estimated from the ANOVA model to assess the degree of dose-proportionality (slope around unity indicates dose-proportionality).

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