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

Title	:	Reporting and Analysis Plan for a single centre, open label, one sequence, cross-over study to evaluate the effect of itraconazole on the pharmacokinetics of single inhaled doses of nemiralisib in healthy volunteers.
Compound Number	:	GSK2269557
Effective Date	:	12-APR-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 206874.
- 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 Statistics Leader (Respiratory Clinical Statistics)	20-MAR-2018	N/A

RAP Team Approvals:

Approver	Date	Approval Method
PPD Manager (Respiratory Clinical Pharmacology Modelling and Simulation)	21-MAR-2018	Electronically within C.A.R.S. system
PPD Clinical Program Lead (Clinical Pharmacology Science and Study Operations)	21-MAR-2018	Electronically within C.A.R.S. system
PPD Physician (Respiratory)	12-APR-2018	Email
PPD Programming Manager (Respiratory Clinical Programming)	20-MAR-2018	Electronically within C.A.R.S. system
PPD Data Quality Lead (Respiratory Data Management)	26-MAR-2018	Electronically within C.A.R.S. system
PPD Medical Director (Global Clinical Safety & Pharmacovigilance)	10-APR-2018	Electronically within C.A.R.S. system

Clinical Statistics and Clinical Programming Line Approvals:

Approver	Date	Approval Method
PPD Director (Respiratory Clinical Statistics)	20-MAR-2018	Electronically within C.A.R.S. system
PPD Manager (Respiratory Clinical Programming)	23-MAR-2018	Electronically within C.A.R.S. system

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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 206874:

Revision Chronology:		
2017N347248_00	12-DEC-2017	Original

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

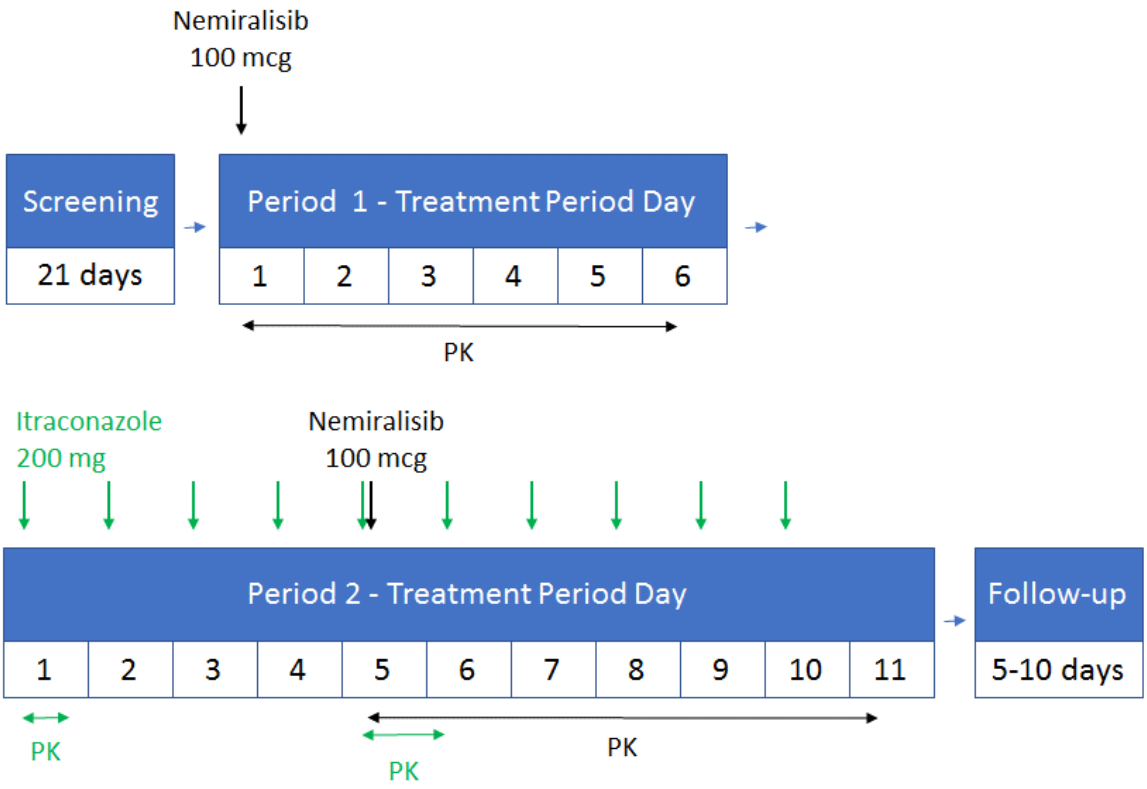
There were no changes or deviations to the originally planned statistical analysis specified in the protocol (Dated: 12/DEC/2017).

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

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To characterize the effect of repeat oral dosing of itraconazole on the pharmacokinetics of a single inhaled dose of GSK2269557 (nemiralisib) in healthy subjects.	• AUC(0-∞) • AUC(0-t) • Cmax • Tmax • $t_{1/2}$
Secondary Objectives	**Secondary Endpoints**
• To investigate the safety and tolerability of single inhaled dose of nemiralisib, when dosed alone and concomitantly with itraconazole, in healthy subjects.	• Adverse events (AE), • Clinical laboratory values, • Vital signs, • Electrocardiogram (ECG) and • Spirometry.
• To investigate the pharmacokinetics of itraconazole and hydroxy itraconazole when co-administered with nemiralisib.	• AUC(0-∞) • AUC(0-t) • Cmax • tmax • $t_{1/2}$

AUC(0-∞) Area under the concentration-time curve from time zero (pre-dose) extrapolated to infinite time, AUC(0-t): Area under the plasma concentration versus time curve from time zero to t, Cmax: maximum observed plasma concentration, tmax: time to Cmax, $t_{1/2}$: Terminal phase half-life.

2.3. Study Design

Overview of Study Design and Key Features	
	
Design Features	• One sequence crossover, open label, single centre. • There will be a washout of at least 14 days between the administration of nemiralisib in Period 1 and the administration of nemiralisib in Period 2. • Subjects will be admitted to the clinical research unit on Day -1 and will remain in-house until collection of the final PK sample in each period. The final PK sample will be Day 6 in Period 1 and Day 11 in Period 2.
Dosing	• Period 1, nemiralisib: On Day 1, subjects will receive a single dose of 100 mcg nemiralisib. • Period 2, itraconazole: From Day 1 to 10 inclusive, subjects will receive a single dose of 200 mg itraconazole in the morning • Period2, nemiralisib: On Day 5, subjects will receive a single dose of 100 mcg nemiralisib one hour after the dose of 200 mg itraconazole. • Participants will receive the administration of nemiralisib on Day 5 and itraconazole doses on Day 5 to Day 10 only if there are no findings that are considered clinically significant by the Investigator (in consultation with the medical monitor if needed) during review of Day 4 clinical chemistry and ECG.
Time & Events	• Refer to Appendix 1: Schedule of Activities.
Treatment Assignment	• All subjects will receive the same treatments in the same periods/on the same study days.
Interim Analysis	• A preliminary assessment of PK will be performed following the availability of the PK data, for internal decision making.

2.4. Statistical Hypotheses / Statistical Analyses

This study is designed to characterise the effect of repeat oral dosing of itraconazole on the pharmacokinetics of a single inhaled dose of nemiralisib in healthy participants. In particular, a comparison will be made between:

- The exposure of nemiralisib administered alone and the exposure of nemiralisib co-administered following repeat doses of itraconazole.

For AUC(0-∞) and Cmax, point estimates and corresponding two-sided 90% confidence intervals (CIs) will be constructed for the ratio of the geometric means. No formal hypotheses will be tested.

3. PLANNED ANALYSES

3.1. Interim Analyses

Following the availability of PK data prior to DBF, a preliminary assessment of unblinded PK data will be performed by CPMS using nominal timepoints. This assessment will be for internal decision making only, will not be formally reported and SAC deliverables will supersede any such output.

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.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants screened and for whom a record exists on the study database.	• Screening Status/Screening Failures
Enrolled	• All participants who passed screening and entered the study. Included are: run-in failures; and participants who took treatment. • Note screening failures and participants screened but never enrolled into the study are excluded from the Enrolled population as they did not enter the study.	• Summary of Study Populations • Summary of Age Ranges
Safety	• All participants enrolled in the study, who took at least one dose of study treatment. • Participants will be analysed according to the treatment they actually received. • Note: Participants who were not assigned treatment but received at least one dose of study treatment should be listed.	• Other Study Population • Safety
Pharmacokinetic (PK)	• All participants enrolled in the study who took at least 1 dose of nemiralisib and for whom a nemiralisib pharmacokinetic sample was obtained and analysed. • Participants will be analysed according to the treatment they received.	• PK

Refer to Appendix 8: 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 in 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	
Data Displays for Reporting	
Description	**Order in TLF**
NEMI 100mcg SD Alone	1
NEMI 100mcg SD with Itraconazole 200mg RD	2

Treatment comparisons will be displayed using the descriptors as follows:

- NEMI 100mcg SD with Itraconazole 200mg RD vs. NEMI 100mcg SD Alone

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions below) the baseline value will be the latest pre-dose assessment with a non-missing value, for the relevant period, 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. Note that baseline for FEV1 is defined as the screening visit in the protocol; however it is not required in any data displays so is not included here.

Parameter	Study Assessments Considered as Baseline		Baseline Used in Data Display
	Screening	Day 1 (Pre-Dose) [Periods 1 and 2]	
Safety			
Vital Signs	X[1]	X	Day 1 predose for the relevant period
ECG	X[1]	X	Day 1 predose for the relevant period

[1] Triplicate

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

5.3. Multiple Comparisons and Multiplicity

No adjustments for multiplicity will be made.

5.4. Other Considerations for Data Analyses and Data Handling Conventions

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

Section	Component
11.2	Appendix 2: Study Phases and Treatment Emergent Adverse Events
11.3	Appendix 3: Data Display Standards & Handling Conventions
11.4	Appendix 4: Derived and Transformed Data
11.5	Appendix 5: Reporting Standards for Missing Data
11.6	Appendix 6: 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 "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 will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 8: List of Data Displays.

7. PHARMACOKINETIC ANALYSES

7.1. Primary Pharmacokinetic Analyses

7.1.1. Endpoint / Variables

7.1.1.1. Drug Concentration Measures

Nemiralisib drug concentration data will be displayed as detailed in Appendix 3: Data Display Standards & Handling Conventions (Section 11.3.3 Reporting Standards for Pharmacokinetic).

7.1.1.2. Derived Pharmacokinetic Parameters

Nemiralisib pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin. All calculations of non-compartmental parameters will be based on actual sampling times. The nemiralisib pharmacokinetic parameters listed below will be determined from the plasma concentration-time data, as data permit.

Parameter	Parameter Description
AUC(0-∞)	Area under the concentration-time curve from zero time (pre-dose) extrapolated to infinite time. AUC(0-∞) = AUC(0-t) + C(t)/λz.
AUC(0-t)	Area under the concentration-time curve from time zero to the time of the last quantifiable concentration
%AUCex	Percentage of AUC(0-∞) obtained by extrapolation
Cmax	Maximum observed plasma concentration
tmax	Time to Cmax
$t_{½}$	Apparent terminal half-life. $t_{1/2} = \ln 2/\lambda z$

NOTES:

- Additional parameters may be included as required.
- λz is the terminal phase rate constant.

7.1.2. Summary Measure

The parameters for treatment comparisons are AUC(0-∞), AUC(0-t), Cmax, tmax and $t_{½}$ for nemiralisib.

7.1.3. Population of Interest

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

7.1.4. Strategy for Intercurrent (Post-Randomization) Events

Two intercurrent events have been identified and will be handled by differing strategies:

- A *while on treatment* strategy will be employed for treatment discontinuation from nemiralisib (i.e. treatment discontinuation prior to dosing with nemiralisib on day 5 of period 2).
- A *hypothetical* strategy will be employed for treatment discontinuation from itraconazole (i.e. treatment discontinuation after dosing with nemiralisib on day 5 of period 2).

7.1.5. Statistical Analyses / Methods

Details of the planned displays for nemiralisib PK data are provided in Appendix 8: List of Data Displays, and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 7.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed. Subjects with greater than 20% extrapolated AUC(0-∞) will be flagged.

7.1.5.1. Statistical Methodology Specification

The following pharmacokinetic statistical analyses for nemiralisib will only be performed if sufficient data is available (i.e. if participants have well defined plasma profiles). If AUC(0-∞) is not calculable for more than 50% of subjects in the PK population in each period, AUC (0-t) will also be analysed for nemiralisib as described below.

Endpoint / Variables
• AUC(0-∞) for nemiralisib • Cmax for nemiralisib
Model Specification
• The parameters AUC(0-∞) and Cmax will be $\log_e$ transformed and analysed separately using mixed effects models. • Treatment Group will be fitted as a fixed effect and subject as a random effect. • The MIXED procedure in SAS will be used with the following options:-   ○ The Kenward and Roger method for approximating the denominator degrees of freedom to correct for bias in the estimated variance-covariance. • Nemiralisib co-administered with itraconazole will be compared to nemiralisib administered alone.
Model Checking & Diagnostics
• Distributional assumptions underlying the models used for analysis will be examined by obtaining box plots and normal probability plots of the studentised residuals and plots 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.
Model Results Presentation
• For each PK parameter:-   • Adjusted geometric means and 90% confidence intervals (CI) for each treatment group and standard error ($\log_e$ scale).

- Point estimates and associated two-sided 90% confidence intervals for the ratio of nemiralisib co-administered with itraconazole to nemiralisib administered alone (obtained by back-transforming estimates and 90% CIs for the treatment differences from the statistical model on the $\log_e$ scale) and standard error ($\log_e$ scale).
- The mean squared error (MSE) will also be presented.

7.2. Secondary Pharmacokinetic Analyses

7.2.1. Endpoint / Variables

7.2.1.1. Drug Concentration Measures

Itraconazole and hydroxy-itraconazole drug concentration data will be displayed as detailed in Appendix 3: Data Display Standards & Handling Conventions (Section 11.3.3 Reporting Standards for Pharmacokinetic).

7.2.1.2. Derived Pharmacokinetic Parameters

The itraconazole and hydroxy-itraconazole plasma pharmacokinetic parameters listed below will be calculated in the same manner as nemiralisib pharmacokinetic parameters – see Section 7.1.1.2.

Parameter	Parameter Description
AUC(0-∞)	Area under the concentration-time curve from zero time (pre-dose) extrapolated to infinite time. AUC(0-∞) = AUC(0-t) + C(t)/λz.
AUC(0-t)	Area under the concentration-time curve from time zero to the time of the last quantifiable concentration
%AUCex	Percentage of AUC(0-∞) obtained by extrapolation
Cmax	Maximum observed plasma concentration
tmax	Time to Cmax
$t_{½}$	Apparent terminal half-life. $t_{1/2} = \ln 2/\lambda z$

NOTES:

- Additional parameters may be included as required.
- λz is the terminal phase rate constant

7.2.2. Summary Measure

The parameters for treatment comparisons are AUC(0-∞), AUC(0-t), Cmax, tmax and $t_{½}$ for both itraconazole and hydroxy-itraconazole.

7.2.3. Population of Interest

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

7.2.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 8: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 7.2.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed. Subjects with greater than 20% extrapolated AUC(0-∞) will be flagged.

No formal statistical analysis will be performed.

8. SAFETY ANALYSES

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

8.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 8: List of Data Displays.

8.2. Adverse Events of Special Interest Analyses

Post-inhalation cough immediately following dosing is an adverse event of special interest (AESI). This will be captured if a participant reports it as an AE. The details of the planned displays are provided in Appendix 8: List of Data Displays.

8.3. 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 8: List of Data Displays.

8.4. Other Safety Analyses

The analyses of non-laboratory safety test results including ECGs and vital signs will be based on GSK Core Data Standards, unless otherwise specified. The details of the planned displays are presented in Appendix 8: List of Data Displays.

9. PHARMACOKINETIC (POPPK)/ PHYSIOLOGICALLY-BASED PK (PBPK) ANALYSES

The study has been designed to capture the NCA pharmacokinetics of nemiralisib alone and when in the presence of itraconazole, to measure the effect, if any, on nemiralisib exposure. If the effect on nemiralisib exposure is large (increased AUC exposure due to markedly decreased clearance) then the sampling regimen may not be adequate for estimation of AUC(0-∞) and a population PK or PBPK approach will be used to estimate AUC(0-∞) of nemiralisib when in the presence of itraconazole. In such case, a separate CPMS RAP will be generated to describe the modelling work prospectively.

9.1. Statistical Analyses / Methods

A summary of the planned potential population pharmacokinetic analyses are outlined below:

- Drug nemiralisib concentration-time data will be subjected to nonlinear mixed effects modelling using the program NONMEM to develop a population PK model or a PBPK approach where more appropriate.
- Individual post-hoc estimated PK parameters will be summarised descriptively.
- To support this analysis a PopPK dataset will be generated.

10. REFERENCES

GlaxoSmithKline Document Number 2017N347248_00 Study ID 206874. A single centre, open label, one sequence, cross-over study to evaluate the effect of itraconazole on the pharmacokinetics of single inhaled doses of nemiralisib in healthy subjects. Report Date 12-DEC-2017.

11. APPENDICES

11.1. Appendix 1: Schedule of Activities

11.1.1. Protocol Defined Schedule of Events

Table 1 Screening and Follow-up

Procedure	Screening (up to 21 days before Day 1)	Follow-up (within 5−10 days of last dose itraconazole)	Notes
Informed consent	X		
Demography	X		
Inclusion and exclusion criteria	X		
Past and current medical conditions	X		
Medical history (includes substance usage)	X		Substances: Drugs, Alcohol, tobacco and caffeine
Physical examination	X	X	Full examination (including height and weight) at screening, brief examination at follow-up
Vital signs	X		Triplicate
12-lead ECG	X	X	Triplicate
FEV_1 and FVC	X		Triplicate
Laboratory assessments (hematology and clinical chemistry)	X	X	
Urinalysis	X		
HIV, Hepatitis B and C screening	X		If test otherwise performed within 3 months prior to first dose of study treatment, testing at screening is not required
Alcohol breath test & drug screen	X		Includes urine cotinine test

Procedure	Screening (up to 21 days before Day 1)	Follow-up (within 5−10 days of last dose itraconazole)	Notes
SAE review	X	X	
AE review		X	

ECG: Electrocardigram, FEV1: Forced expiratory volume in 1 second, FVC: Forced vital capacity, HIV: Human immunodeficiency virus, AE: Adverse event, SAE: Serious adverse event.

Table 2 Period 1

Procedure	Treatment Period Days							Notes
	–1	1	2	3	4	5	6	
Admission	X							
Discharge							X	
Alcohol breath test & drug screen	X							Includes urine cotinine test
Laboratory assessments (hematology, clinical chemistry and urinalysis)	X						X	Day −1 results to be reviewed before dosing on Day 1
Brief physical examination	X						X	
Inhaler (Ellipta™) training	X							Training conducted by reviewing the Patient Information Leaflet with the participant. Additional training may be conducted at the discretion of the investigator.
FEV_1	X							Triplicate.
12-lead ECG		X					X	Single measurement. Pre-dose on Day 1.
Vital signs		X					X	Single measurement. Pre-dose on Day 1.
Study treatment (nemiralisib)		X						
Pharmacokinetic (PK) (nemiralisib)		X	X	X	X	X	X	pre-dose, and 5 min, 30 min, 2 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h and 120 h post-dose
AE review		←==========					→	
SAE review	X	←==========					→	
Concomitant medication review	X	←==========					→	

Table 3 Period 2

Procedure	Treatment Period Days												Notes
	–1	1	2	3	4	5	6	7	8	9	10	11	
Admission	X												
Discharge												X	
Alcohol breath test & drug screen	X												Includes urine cotinine test
Brief physical examination	X											X	
Laboratory assessments (hematology, clinical chemistry and urinalysis)	X										X		Pre-dose at all timepoints. Day −1 results to be reviewed before dosing on Day 1.
Clinical chemistry only			X		X		X		X				Pre-dose at all timepoints. Day 4 results to be reviewed before itraconazole dosing on Day 5.
12-lead ECG		X	X		X		X		X		X		Single measurement. Pre-dose and 3h post-dose (itraconazole) on Day 1. Pre-dose at all other timepoints, Day 4 results to be reviewed before itraconazole dosing on Day 5.
Vital signs		X	X		X		X		X		X		Single measurement. Pre-dose at all timepoints
Study treatment (itraconazole)		X	X	X	X	X	X	X	X	X	X		Approx. 1 h post standard meal.
FEV_1					X								Triplicate
Inhaler (Ellipta) training					X								Training conducted by reviewing the Patient Information Leaflet with the participant. Additional training may be conducted at the discretion of the investigator.
Study treatment (nemiralisib)						X							1 h post itraconazole administration.
PK (nemiralisib)						X	X	X	X	X	X	X	pre-dose, and 5 min, 30 min, 2 h, 6 h, 12 h, 24 h, 48 h, 72 h, 96 h, 120 h and 144 h post-dose (nemiralisib)

Procedure	Treatment Period Days												Notes
	–1	1	2	3	4	5	6	7	8	9	10	11	
PK (itraconazole + hydroxy-itraconazole)		X				X	X						Pre-dose, 30 min, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, 12 h post-dose (itraconazole) on Day 1 Pre-dose, 30 min, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, 12 h and 24 h hours post-dose (itraconazole) on Day 5
AE review		←==========→											
SAE review	X	←==========→											
Concomitant medication review	X	←==========→											

- The timing and number of planned study assessments, including safety and pharmacokinetic assessments 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 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 Institutional review board (IRB)/ Independent ethics committee (IEC) will be informed of any safety issues that require alteration of the safety monitoring scheme or amendment of the Informed consent form (ICF).

11.2. Appendix 2: Study Phases and Treatment Emergent Adverse Events

11.2.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is prior to screening visit
Concomitant	Any medication that is not a prior

NOTES:

- Please refer to Appendix 5: Reporting Standards for Missing Data for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

11.2.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	• If AE onset date is on or after study treatment start date (for that period) & on or before nemiralisib treatment stop date (for that period) plus 10 days (5 times half life of nemiralisib). • Study Treatment Start Date (for that period) ≤ AE Start Date ≤ Nemiralisib Treatment Stop Date (for that period) + 10 days . • Where 'study treatment' start date (for that period) refers to the date of the first dose given in that period (i.e. nemiralisib for period 1 and itraconazole for period 2)

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.

11.3. Appendix 3: Data Display Standards & Handling Conventions

11.3.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: uk1salx00175
HARP Compound	: GSK2269557/mid206874
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version v3.2 & ADaM IG Version 1.0.	
Generation of RTF Files	
• RTF files will be generated for the final reporting effort.	

11.3.2. 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 summary figures, summaries, statistical analyses and calculation of any derived parameters.
  • Actual relative time will be used in subject plots and for the derivation of PK parameters.
  • 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 or figures. • All unscheduled visits will be included in listings.

Listings	
• Since this is a single sequence study, there is no need to include 'Sequence' or 'Arm' in any of the 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 Principles 7.01 to 7.13.	

11.3.3. 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 Modelling and Simulation function will be created according to PK IDSL Standards. 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 and summarized graphical displays only. The number of values imputed will be included as a column in the summary tables.
NONMEM/Pop PK File	Not applicable.
NONMEM/PK/PD File	Not applicable.
Pharmacokinetic Parameter Derivation	
PK Parameters to be Derived by Programmer	None
Pharmacokinetic Parameter Data	
Is the 'NQ impacted PK Parameters' Rule Being Followed?	Yes, refer to Standards for Handling NQ Impacted PK Parameters.
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards.

11.4. Appendix 4: Derived and Transformed Data

11.4.1. General

Multiple Measurements at One Analysis Time Point
• The 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 within the period in question (in period 1 this will be the date of dosing with nemiralisib; in period 2 this will be the date of first dosing with itraconazole):
  • 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

11.4.2. Study Population

Demographics
Age

• GSK standard algorithms will be used for calculating age where birth date is imputed as:
  • Any subject with a missing day will have this imputed as day '15'.
  • Any subject with a missing date and month will have this imputed as '30th June'.
  • Birth date will be presented in listings as 'YYYY'.

Body Mass Index (BMI)
• Calculated as Weight (kg) / [Height (m)]^2

Extent of Exposure
• Number of days of exposure to each study drug will be calculated for each period based on the formula: **Duration of Exposure in Days = Treatment Stop Date – (Treatment Start Date) + 1** • Participants who were assigned treatment but did not report a treatment start date will be categorised as having zero days of exposure. • The cumulative dose will be based on the formula: **Cumulative Dose = Sum of (Number of Days x Total Daily Dose)** • If there are any treatment breaks during the study, exposure data will be adjusted accordingly.

11.4.3. Safety

Adverse Events
AE Time Since First Dose (Days)
• If AE start date/time < date/time of first dose then Time since first dose = date of first dose – AE start date • If AE start date/time ≥ date/time of first dose then Time since first dose = AE start date – date of first dose+1 • Missing if AE start date or date of first dose is missing. • Note: First dose will be the date of dosing with nemiralisib in period 1 and the date of first dosing with itraconazole in period 2.
AE Duration (Days)
• AE end date – AE start date + 1 • Missing if AE start date or end date is missing.
AE's of Special Interest
• Post-inhalation cough is an AE of special interest. The lower level term (LLT) to be included is "coughing after drug inhalation"

11.5. Appendix 5: Reporting Standards for Missing Data

11.5.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as completing all phases of the study including the last visit. • 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.

11.5.2. 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 output. ○ Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such. ○ Data below the limit of quantification (BLQ) is not missing data and must be displayed as 'NQ (< x)' where x is the lower limit of quantification, and included in all listings and summaries. ○ Analysis will be performed on all available data and no imputation will be performed for missing data.
Outliers	• Any participants excluded from the summaries and/or statistical analyses because their values are considered outliers will be documented along with the reason for exclusion in the clinical study report.

11.5.2.1. 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: ○ 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 2: Study Phases and Treatment Emergent Adverse Events. ○ 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. ○ Note: start date and stop dates are defined as the first/last dose given in the period, regardless of whether it is nemiralisib or itraconazole. • Completely missing start or end dates will remain missing, with no imputation applied.

Element	Reporting Detail
	Consequently, time to onset and duration of such events will be missing.
Concomitant Medications/ Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month o 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.

11.6. Appendix 6: Values of Potential Clinical Importance

11.6.1. Laboratory Values

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Hematocrit	%	Male	35	60
		Female	35	60
		Δ from BL	↓7.5	
Haemoglobin	g/L	Male	130	180
		Female	120	170
		Δ from BL	↓25	
Lymphocytes	$x10^9$/ L		0.8	4.0
Neutrophil Count	$x10^9$/ L		1.5	12.0
Platelet Count	$x10^9$/ L		100	600
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)**
Total Protein	g/L		55	90
Calcium	mmol/L		2	2.75
Creatinine	µmol/L			1.3 x ULN
Glucose	mmol/L		3	9
Magnesium	mmol/L		0.7	1.25
Phosphorus	mmol/L		0.8	1.6
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	155

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

11.6.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTcF Interval	msec	≤ 300	≥ 450
Absolute PR Interval	msec	< 100	>240
Absolute Ventricular Rate	beats/min	<35	>100
Change from Baseline			
Increase from Baseline QTcF	msec		>60

11.6.3. Vital Signs

Vital Sign Parameter (Absolute)	Units	Clinical Concern Range	
		Lower	Upper
Systolic Blood Pressure	mmHg	≤ 90	≥ 150
Diastolic Blood Pressure	mmHg	≤ 40	≥ 100
Heart Rate	bpm	≤ 35	≥ 100
Respiration rate	breaths/min	≤ 8	≥ 20
Oral Temperature	ºC	≤ 35.5	≥ 37.5

11.7. Appendix 7: Abbreviations & Trade Marks

11.7.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AESI	Adverse Event of Special Interest
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
BLQ	Below Limit of Quantification
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
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
PBPK	Physiologically Based PK
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
PopPK	Population PK
QC	Quality Control
QTcF	Fridericia's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan

Abbreviation	Description
RAMOS	Randomization & Medication Ordering System
SAC	Statistical Analysis Complete
SDSP	Study Data Standardization Plan
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
TA	Therapeutic Area
TFL	Tables, Figures & Listings
WNL	Windows Non-Linear

11.7.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
None

Trademarks not owned by the GlaxoSmithKline Group of Companies
NONMEM
SAS
WinNonlin

11.8. Appendix 8: List of Data Displays

11.8.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.9	
Pharmacokinetic	2.1 to 2.10	2.1 to 2.10
Safety	3.1 to 3.10	
Section	**Listings**	
ICH Listings	1 to 32	
Other Listings	33 to 39	

11.8.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 9: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln

NOTES:

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

11.8.3. Deliverables

Delivery	Description
SAC	Final Statistical Analysis Complete

11.8.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Safety	ES1A	Summary of Participant Disposition for the Participant Conclusion Record	ICH E3, FDAAA, EudraCT	SAC
1.2.	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment	ICH E3	SAC
1.3.	Safety	ES4	Summary of Participant Disposition at Each Study Period	ICH E3	SAC
1.4.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements	SAC
Protocol Deviation					
1.5.	Safety	DV1	Summary of Important Protocol Deviations	ICH E3	SAC
Population Analysed					
1.6.	Enrolled	SP1A	Summary of Study Populations	IDSL Total column only	SAC
Demographic and Baseline Characteristics					
1.7.	Safety	DM3	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	SAC
1.8.	Enrolled	DM11	Summary of Age Ranges	EudraCT	SAC
1.9.	Safety	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT	SAC

11.8.5. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration					
2.1.	PK	PK01	Summary of Nemiralisib Plasma Concentration-Time Data	Include footnote: 'Times are relative to dosing with nemiralisib'.	SAC
2.2.	PK	PK01	Summary of Itraconazole Plasma Concentration-Time Data (Period 2)	Still include treatment group as a variable Include footnote: 'Times are relative to dosing with itraconazole'.	SAC
2.3.	PK	PK01	Summary of Hydroxy Itraconazole Plasma Concentration-Time Data (Period 2)	Still include treatment group as a variable Include footnote: 'Times are relative to dosing with itraconazole'.	SAC
PK Parameter					
2.4.	PK	PK03	Summary of Untransformed Derived Nemiralisib Plasma Pharmacokinetic Parameters	Don't include 95% CI Include variable 'day' If any NC values, include n* column and add footnote: 'NOTE: n*=number of NC values'. Include footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.5.	PK	PK05	Summary of Log-transformed Derived Nemiralisib Plasma Pharmacokinetic Parameters	Include all parameters except %AUCex and tmax Include variable 'day'. If any NC values, include n* column and add footnote: 'NOTE: n*=number of NC values'. Include footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
2.6.	PK	PK03	Summary of Untransformed Derived Itraconazole Plasma Pharmacokinetic Parameters (Period 2)	Don't include 95% CI. Still include treatment group as a variable. Include variable 'day'. If any NC values, include n* column and add footnote: 'NOTE: n*=number of NC values'. Include footnote: 'Nemiralisib was administered on Day 5 of Period 2.'	SAC
2.7.	PK	PK05	Summary of Log-transformed Derived Itraconazole Plasma Pharmacokinetic Parameters (Period 2)	Include all parameters except %AUCex and tmax Still include treatment group as a variable. Include variable 'day' If any NC values, include n* column and add footnote: 'NOTE: n*=number of NC values'. Include footnote: 'Nemiralisib was administered on Day 5 of Period 2.'	SAC

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.8.	PK	PK03	Summary of Untransformed Derived Hydroxy Itraconazole Plasma Pharmacokinetic Parameters (Period 2)	Don't include 95% CI. Still include treatment group as a variable. Include variable 'day'. If any NC values, include n* column and add footnote: 'NOTE: n*=number of NC values'. Include footnote: 'Nemiralisib was administered on Day 5 of Period 2.'	SAC
2.9.	PK	PK05	Summary of Log-transformed Derived Hydroxy Itraconazole Plasma Pharmacokinetic Parameters (Period 2)	Include all parameters except %AUCex and tmax Still include treatment group as a variable. Include variable 'day'. If any NC values, include n* column and add footnote: 'NOTE: n*=number of NC values'. Include footnote: 'Nemiralisib was administered on Day 5 of Period 2.'	SAC
2.10.	PK	Non Standard PK_T1	Summary of Statistical Analysis of Derived Nemiralisib Plasma AUC(0-inf) and Cmax	AUC(0-inf) and Cmax only (unless AUC(0-t) also analysed) Include MSE Include n* and footnote (in shell) if there are any NC values	SAC

11.8.6. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration					
2.1.	PK	PK16b	Individual Nemiralisib Plasma Concentration-Time Plots (Linear and Semi-Log) by Subject	Separate plots per subject Add a horizontal dashed line at y-axis = 5 pg/mL and footnote: LLQ = 5 pg/mL	SAC
2.2.	PK	PK24	Individual Nemiralisib Plasma Concentration-Time Plots (Linear and Semi-Log) by Treatment Group	All subjects in the same treatment group on the same graph ("spaghetti plot"). Separate page per treatment. Add a horizontal dashed line at y-axis = 5 pg/mL and footnote: LLQ = 5 pg/mL	SAC
2.3.	PK	PK17	Mean Nemiralisib Plasma Concentration-Time Plots (Linear and Semi-Log) by Treatment Group	Add a horizontal dashed line at y-axis = 5 pg/mL and footnote: LLQ = 5 pg/mL	SAC
2.4.	PK	PK18	Median Nemiralisib Plasma Concentration-Time Plots (Linear and Semi-Log) by Treatment Group	Add a horizontal dashed line at y-axis = 5 pg/mL and footnote: LLQ = 5 pg/mL	SAC
2.5.	PK	PK24	Individual Itraconazole Plasma Concentration-Time Plots (Linear and Semi-Log) by Treatment Group (Period 2)	All subjects on the same graph ("spaghetti plot"). Still include treatment group Add a horizontal dashed line at y-axis = 2 ng/mL and footnote: LLQ = 2 ng/mL Add footnote: 'Nemiralisib was administered on Day 5 of Period 2.'	SAC

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.6.	PK	PK19	Mean (±SD) Itraconazole and Hydroxy-Itraconazole Plasma Concentration-Time Plots (Linear and Semi-Log) by Treatment Group (Period 2)	Both itraconazole and hydroxy-itraconazole on the same plot. +SD for itraconazole and -SD for hydroxy-itraconazole. Add a horizontal dashed line at y-axis = 2 ng/mL and footnote: LLQ = 2 ng/mL. Still include treatment group Add footnote: 'Nemiralisib was administered on Day 5 of Period 2.'	SAC
2.7.	PK	PK18	Median Itraconazole and Hydroxy-Itraconazole Plasma Concentration-Time Plots (Linear and Semi-Log) by Treatment Group (Period 2)	Both itraconazole and hydroxy-itraconazole on the same plot Add a horizontal dashed line at y-axis = 2 ng/mL and footnote: LLQ = 2 ng/mL Still include treatment group Add footnote: 'Nemiralisib was administered on Day 5 of Period 2.'	SAC
2.8.	PK	PK24	Individual Hydroxy-Itraconazole Plasma Concentration-Time Plots (Linear and Semi-Log) by Treatment Group (Period 2)	All subjects on the same graph ("spaghetti plot"). Still include treatment group Add a horizontal dashed line at y-axis = 2 ng/mL and footnote: LLQ = 2 ng/mL Add footnote: 'Nemiralisib was administered on Day 5 of Period 2.'	SAC

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Parameter					
2.9.	PK	PK28	Individual Subject (+Geometric Mean and 90% CI) Derived Nemiralisib Plasma PK Parameters by Treatment Group	AUC(0-inf) and Cmax only (unless AUC(0-t) also analysed) Each parameter on a separate page All subjects to be indicated with an 'x' The two treatment groups on the x-axis Parameter values on a log scale on y-axis	SAC
2.10.	PK	Non Standard PK_F1	Treatment Ratios (90% CIs) for Analysis of Derived Nemiralisib Plasma AUC(0-inf) and CMax	AUC(0-inf) and Cmax only (unless AUC(0-t) also analysed) All parameters on the x-axis of the same plot. Ratio on a log scale on y-axis	SAC

11.8.7. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	Safety	AE1CP /	Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3	SAC
3.2.	Safety	AE1CP	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term	ICH E3	SAC
Laboratory: Chemistry					
3.3.	Safety	LB1	Summary of Chemistry Changes from Baseline	ICH E3 Include baseline values. Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2'.	SAC
Laboratory: Hematology					
3.4.	Safety	LB1	Summary of Hematology Changes from Baseline	ICH E3 Include baseline values. Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2'.	SAC
Laboratory: Urinalysis					
3.5.	Safety	UR3b	Summary of Urine Dipstick Results	ICH E3 Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2'.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Hepatobiliary (Liver)					
3.6.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting	IDSL	SAC
3.7.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities	IDSL	SAC
ECG					
3.8.	Safety	EG1	Summary of ECG Findings	IDSL Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2	SAC
3.9.	Safety	EG2	Summary of Change from Baseline in ECG Values by Visit	IDSL Include baseline values. Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2'.	SAC
Vital Signs					
3.10.	Safety	VS1	Summary of Change from Baseline in Vital Signs	ICH E3 Include baseline values. Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2'.	SAC

11.8.8. 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 Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.	SAC
3.	Safety	SD3	Listing of Reasons for Study Treatment Discontinuation	ICH E3 Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.	SAC
4.	Enrolled	CP_RA1x	Listing of Planned and Actual Treatments	IDSL Only include the following variables: Site ID, Subject, Period, Planned Treatment, Actual Treatment	SAC
Protocol Deviations					
5.	Safety	DV2A	Listing of Important Protocol Deviations	ICH E3	SAC
6.	Safety	IE4	Listing of Participants with Inclusion/Exclusion Criteria Deviations	ICH E3	SAC
Populations Analysed					
7.	Enrolled	SP3a	Listing of Participants Excluded from Any Population	ICH E3	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Demographic and Baseline Characteristics					
8.	Safety	DM4	Listing of Demographic Characteristics	ICH E3	SAC
9.	Safety	DM10	Listing of Race	ICH E3	SAC
Concomitant Medications					
10.	Safety	CP_CM4	Listing of Concomitant Medications	IDSL	SAC
Exposure					
11.	Safety	EX4	Listing of Nemiralisib Exposure Data	ICH E3 Include Period, Start Period Day (under study day), Stop Period Day (under study day). Don't include Cumulative Dose. Dosing Frequency = 'OD'	SAC
12.	Safety	EX4	Listing of Itraconazole Exposure Data	ICH E3 Include Period, Start Period Day (under study day), Stop Period Day (under study day), Cumulative Dose Dosing Frequency = 'OD'	SAC
Adverse Events					
13.	Safety	AE9CP	Listing of All Adverse Events	ICH E3 Drop 'Maximum Grade' variable Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
14.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	SAC
15.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	SAC
Serious and Other Significant Adverse Events					
16.	Safety	AE9CPA	Listing of Serious Adverse Events	ICH E3 Drop 'Maximum Grade' variable Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
17.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	SAC
18.	Safety	AE9CP	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3 Drop 'Maximum Grade' variable Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
Adverse Events of Special Interest					
19.	Safety	AE9CP	Listing of Adverse Events Categorised as Post Inhalation Cough	Drop 'Maximum Grade' variable Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
Hepatobiliary (Liver)					
20.	Safety	MH2	Listing of Medical Conditions for Participants with Liver Stopping Events	IDSL	SAC
21.	Safety	SU2	Listing of Substance Use for Participants with Liver Stopping Events	IDSL	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
All Laboratory					
22.	Safety	LB6	Listing of All Chemistry Data for Participants with Any Value of Potential Clinical Importance	ICH E3 Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
23.	Safety	LB6	Listing of All Hematology Data for Participants with Any Value of Potential Clinical Importance	ICH E3 Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
24.	Safety	LB6	Listing of Chemistry Values of Potential Clinical Importance	Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
25.	Safety	LB6	Listing of Hematology Values of Potential Clinical Importance	Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
26.	Safety	LB14	Listing of Laboratory Data with Character Results	ICH E3 Include Treatment/Period and sort as for a crossover study. Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
ECG					
27.	Safety	EG4	Listing of All ECG Values for Participants with Any Value of Potential Clinical Importance	IDSL Include actual relative time. Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
28.	Safety	EG4	Listing of ECG Values of Potential Clinical Importance	IDSL Include actual relative time. Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
29.	Safety	EG6	Listing of All ECG Findings for Participants with an Abnormal ECG Finding	IDSL Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
30.	Safety	EG6	Listing of Abnormal ECG Findings	IDSL Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
Vital Signs					
31.	Safety	VS5	Listing of All Vital Signs Data for Participants with Any Value of Potential Clinical Importance	IDSL Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
32.	Safety	VS5	Listing of Vital Signs of Potential Clinical Importance	IDSL Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC

11.8.9. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
FEV_1					
33.	Safety	PFT10	Listing of FEV1 and FVC Data	Include Treatment, Period, Day In terms of FEV1 and FVC, only need Max FEV1, Max FVC, % Predicted FEV1, % Predicted FVC Add Footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
PK Concentration					
34.	PK	PK08	Listing of Nemiralisib Plasma Concentration-Time Data	Add footnote: 'Times are relative to dosing with nemiralisib'.	SAC
35.	PK	PK08	Listing of Itraconazole Plasma Concentration-Time Data (Period 2)	Still include treatment group as a variable. Add footnote: 'Times are relative to dosing with itraconazole'.	SAC
36.	PK	PK08	Listing of Hydroxy Itraconazole Plasma Concentration-Time Data (Period 2)	Still include treatment group as a variable. Add footnote: 'Times are relative to dosing with itraconazole'.	SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Parameter					
37.	PK	PK14	Listing of Derived Nemiralisib Pharmacokinetic Parameters	Include the variable 'day'. Flag AUC(0-inf) for subjects with >20%AUCex with a *. Add footnote:'*: Greater than 20% of AUC(0-inf) obtained by extrapolation'. Add footnote: 'Nemiralisib was administered on Day 1 of Period 1 and Day 5 of Period 2.'	SAC
38.	PK	PK14	Listing of Derived Itraconazole Pharmacokinetic Parameters (Period 2)	Include the variable 'day'. Still include treatment group as a variable. Flag AUC(0-inf) for subjects with >20%AUCex with a *. Add footnote:'*: Greater than 20% of AUC(0-inf) obtained by extrapolation'. Add footnote: 'Nemiralisib was administered on Day 5 of Period 2.'	SAC
39.	PK	PK14	Listing of Derived Hydroxy Itraconazole Pharmacokinetic Parameters (Period 2)	Include the variable 'day'. Still include treatment group as a variable. Flag AUC(0-inf) for subjects with >20%AUCex with a *. Add footnote:'*: Greater than 20% of AUC(0-inf) obtained by extrapolation'. Add footnote: 'Nemiralisib was administered on Day 5 of Period 2.'	SAC

11.9. Appendix 9: Example Mock Shells for Data Displays

Data Display Specification will be made available on Request