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

Title	:	Reporting and Analysis Plan for a Randomized double blind (sponsor unblind) study evaluating the effect of 14 days of treatment with danirixin (GSK1325756) on neutrophil extracellular traps (NETs) formation in participants with stable chronic obstructive pulmonary disease (COPD)
Compound Number	:	GSK1325756
Effective Date	:	14-NOV-2018

Description:

- The purpose of this RAP is to describe planned efficacy and safety analyses and output to be included in the Clinical Study Report (CSR) for Protocol 207551.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.

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1. INTRODUCTION

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

Revision Chronology:		
2017N314013_00	16-MAY-2017	Original

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
• Enrolled - All participants who sign informed consent	• Enrolled - All participants who sign informed consent and for whom a record exists on the study database	• Align with standard Enrolled population definition.
• Randomised	• mITT population defined to be used for selected displays	• Used for key displays
• Primary completer	• Population definition refined	• To allow for missing data and increase clarity
• Safety	• mITT population used for safety reporting	• Safety population not required.
• PK population	• PK population defined	• Used for PK displays
• Endpoint - Model specific PK parameters of danirixin (e.g., oral clearance, oral steady state volume of distribution).	• Danirixin concentration and standard pharmacokinetic (PK) parameters for danirixin (e.g. AUC, Cmax, tmax)	• Updated due to small number of participants with PK data
• Endpoints - serum IL-8 or sputum mucin	• Removed	• Not collected
• Primary analysis Bayesian	• Primary analysis Frequentist	• The primary analysis has been simplified as the historical data could not be used as a prior.
• Modified Primary Completer	• Population defined	• Defined to allow for a sensitivity around the definitions of quality for the samples

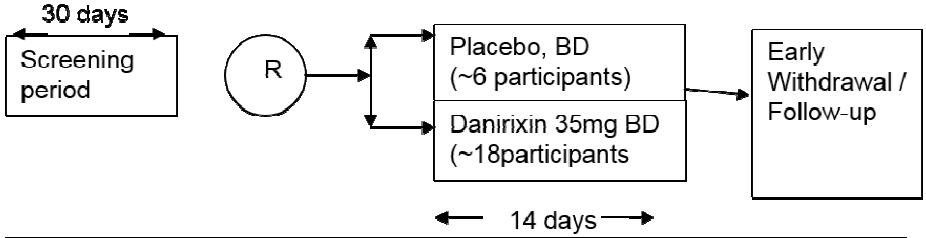
2.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To assess the change from baseline in NETs formation in participants with COPD following 14 days of treatment with danirixin hydrobromide (HBr) 35mg twice daily	• Reduction in sputum NETs (quantified by Histone-elastase complexes)
Secondary Objectives	**Secondary Endpoints**
• To assess the change from baseline in NETs formation in participants with COPD following 14 days of treatment with danirixin HBr 35mg twice daily	• Reduction in sputum NETS (quantified by Deoxyribonucleic acid [DNA]-elastase complexes) • Reduction in sputum NET area quantification by microscopy
• To further characterize the safety of danirixin HBr 35mg tablets compared with placebo in participants with COPD	• Adverse events • Vital Signs • ECG • Spirometry
• To assess the effects of danirixin HBr 35mg twice daily on NETosis-associated biomarkers in sputum and peripheral blood	• Change from baseline in sputum resistin levels • Change from baseline in the ratio of sputum NETs to sputum neutrophils • Change from baseline in sputum elastase activity • Change from baseline in peripheral blood neutrophil NET formation (DNA release)
• Characterise the population pharmacokinetic (PK) profile of approximately 14 days of dosing of danirixin HBr 35mg twice daily in participants with COPD	• Danirixin concentration and standard pharmacokinetic (PK) parameters for danirixin (e.g. AUC, Cmax, tmax)
Exploratory Objectives	**Exploratory Endpoints**
• To explore the relationships between NETs formation and lung microbiome composition	• Characterize sputum microbiome composition and diversity
• To explore volatile organic compound (VOC) profile in participants with COPD	• Characterize relationship between lung microbiome and exhaled volatile organic compounds (VOCs) in stable COPD • To explore variability of exhaled VOCs
• To explore the effects of danirixin	• Changes from baseline in ex-vivo neutrophil

Objectives	Endpoints
HBr 35mg twice daily on neutrophil activity and exploratory biomarkers	phagocytosis of bacteria by flow cytometry • Changes in exploratory urine, sputum and blood biomarkers (e.g. plasma fibrinogen, serum C-reactive protein)

2.3. Study Design

Overview of Study Design and Key Features



*R=Randomization
Notes:
•Early Withdrawal visit to occur as soon as possible (ASAP) after decision to withdraw by either investigator or participant
•Follow up phone-call to occur within 7 days of last dose of study medication

Design Features	• Single centre, randomized, double-blind, sponsor open, placebo-controlled, 14-day mechanistic study evaluating the effect of danirixin in reducing NET formation.
Dosing	• Study treatment will be administered twice daily for 14 days.
Treatment Assignment	• Participants will be randomized (3:1) to receive either danirixin HBr 35mg or placebo. • GSK RandAll NG used to generate randomisation schedules.
Interim Analysis	• No formal interim analysis will be preformed

2.4. Statistical Hypotheses / Statistical Analyses

The objective of this study is to assess whether danirixin impacts NET formation in participants with COPD. There will be no formal hypotheses tests and significant tests. Model based results for the primary endpoint of reduction in sputum NETs (quantified by Histone-elastase complexes) adjusted for baselin, will be used.

3. PLANNED ANALYSES

3.1. Interim Analyses

There is no formal interim analysis planned for this study. Although, blinded data looks were performed at 12 participants and 19 participants. The purpose of the data looks is to check data quality. The data showed that 6 participants had poor quality data. The team decided to replace all 6 participants; approximately 30 participants will be enrolled.

3.2. Final Analyses

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

1. After decision to terminate DNX in COPD the study was stopped early. 19 subjects had completed the study.
2. All required database cleaning activities have been completed and final database release (DBR)
3. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed according to RandAll NG procedures.
5. Database freeze (DBF) has been declared by Data Management.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Enrolled	All participants who sign informed consent and for whom a record exists on the study database. This population will be used for the tables/listings of reasons for withdrawal before randomization and listings of AEs and SAEs for non-randomized participants.	• Subject Disposition • Reasons for withdrawal before randomization. • Inclusion, exclusion, and randomization criteria deviations
Modified ITT	All randomized participants who receive at least one dose of study treatment. Participants will be analysed according to the treatment they actually received. If a participant received more than one treatment during the treatment period, they will be reported according to the treatment taken the most based on doses taken from each container.	• Study population • Efficacy • Safety
Primary Completer	All participants in the Modified ITT population who have completed the assessments supporting the primary endpoint (sputum NETs). • In the case where the modified ITT and the primary completer population are the	• Sputum NETs • Secondary NETs analyses

Population	Definition / Criteria	Analyses Evaluated
	same, the primary completer population will not be defined and all output will be done on the Modified ITT population. • Participants need sputum samples of acceptable quality at screening/baseline and day 14. • Acceptable quality samples have viable leukocytes >50% and coded as acceptable or good in MISPQL	
Modified Primary Completer	All participants in the Modified ITT population who have completed the assessments supporting the primary endpoint (sputum NETs). • In the case where the modified ITT and the primary completer population are the same, the primary completer population will not be defined and all output will be done on the Modified ITT population. • Participants need sputum samples of reasonable quality at screening/baseline and day 14. Reasonable quality samples have viable leukocytes >50% and coded as acceptable, good or poor quality in MISPQL This population will only be use if this increases the available sample from the Primary completer population by 20%.	• Secondary NETs analyses
PK	All participants in the mITT population who had at least 1 non-missing PK assessment (Non-quantifiable [NQ] values will be considered as non-missing values) obtained and analysed whilst on treatment with danirixin.	• PK

NOTES : Please refer to Appendix 11: List of Data Displays which details the population to be used for each displays being generated.

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 17Aug2017 Final V1.0.

- 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 System		**Data Displays for Reporting**	
Code	**Description**	**Description**	**Order in TLF**
PBO	Placebo	Placebo	1
DNX	GSK1325756 (danirixin) 35mg HBr	DNX 35mg BD	2

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

1. Danirixin vs. Placebo

5.2. Baseline Definitions

Parameter	Study Assessments Considered as Baseline		Baseline Used in Data Display
	Screening (Visit 0 / Visit 1)	Day 1 (Visit 2)	
Induced sputum variables	X	X	Baseline
Vital signs		X	Baseline
Spirometry variables		X	Baseline
ECG [mean of triplicate]		X	Baseline
Clinical Laboratory Assessments		X	Baseline

For labs, vitals and ECG, use the most recent value prior to dosing. In cases where the induced sputum from day 1 does not meet quality standards, the sample from screening can be used.

5.3. Examination of Covariates, Other Strata and Subgroups

5.3.1. Covariates and Other Strata

Other covariates will be included for specific analyses as detailed in model specifications in Section 7.1 and Section 7.2.

Category	Details
Covariates	Treatment, baseline

5.4. Multiple Comparisons and Multiplicity

No adjustment for multiplicity is required for this study, as the primary analysis involves an estimation approach, rather than hypothesis testing.

5.5. 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
12.3	Appendix 3: Assessment Windows
12.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
12.5	Appendix 5: Data Display Standards & Handling Conventions
12.6	Appendix 6: Derived and Transformed Data
12.7	Appendix 7: Reporting Standards for Missing Data
12.8	Appendix 8: 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 modified ITT 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 11: List of Data Displays.

7. EFFICACY ANALYSES

7.1. Primary Efficacy Analyses

7.1.1. Endpoint / Variables

The primary endpoint will be the percent change (relative to baseline) in sputum NETs, quantified by Histone-elastase complexes, for danirixin.

7.1.2. Summary Measure

Mean and 95% confidence interval will be calculated for the danirixin and placebo arms at day 7 and 14.

7.1.3. Population of Interest

The primary efficacy analysis will be based on the Primary Completer population, unless the primary completer populations is the same as the mITT population. In that case the mITT population will be used for all analysis. Participants with poor quality sputum samples should also be excluded from the analysis.

7.1.4. Strategy for Intercurrent (Post-Randomization) Events

No intercurrent events are considered of interest in this analysis. Data for the endpoint will be complete for the specific population

7.1.5. Statistical Analyses / Methods

Unless otherwise specified, endpoints / variables defined in Section 7.1.1 will be summarised using descriptive statistics, graphically presented and listed.

7.1.5.1. Statistical Methodology Specification

Endpoint / Variables
• Sputum NETs quantified by Histone-elastase complexes
Model Specification
• The ratio of post-baseline NETs values to baseline NETS values will be log transformed prior to analysis. Note: $\log\left(\frac{NETs_{post}}{NETs_{baseline}}\right) = \log(NETs_{post}) - \log(NETs_{baseline})$. • $y_{ij} = \beta_{baseline} \cdot \log(x_i) + \beta_{treatment} \cdot x_i + \beta_{day\ xtreatment} \cdot x_{ij} + \gamma_i + \epsilon_{ij}$ • Where i is the index for each participant and j is the index for day
Model Checking & Diagnostics
• The mixed effect model will control for treatment, baseline, and day. • An unstructured symmetric covariance structure will be used. Although if there are issues with convergence auto-regressive lag 1 can be used. • It may be necessary to exclude placebo data from the analysis due to small cell size. • The Kenward and Rodger method for approximating the denominator degrees of freedom and

correcting for bias in the estimated variance-covariance of the fixed effects will be used • If there are any departure from the distributional assumptions, alternative models will be explored using appropriate transformed data. Residual plots will be checked.
Model Results Presentation
• Refer to Appendix 12 for detailed description of tables, figures, and listings

7.2. Secondary Efficacy Analyses

7.2.1. Endpoint / Variables

The endpoint will be the change (relative to baseline) in sputum NETs, quantified by DNA-elastase and microscopy sputum resistin levels, ratio of sputum NETs to sputum neutrophils, sputum neutrophils, and sputum elastase activity. The mapping to dataset values are as follows. NETs quantified by microscopy are mean percent NETs per field. For a mapping of protocol variables to dataset variables (see Dataset to Protocol Mapping)

7.2.2. Summary Measure

Unadjusted mean and standard error will be calculated for the danirixin and placebo arms at baseline, day 7 and 14. Unadjusted mean and standard error will be calculated for the percent change from baseline and absolute change from baseline for danirixin and placebo arms at day 7 and 14.

7.2.3. Population of Interest

Same as above, for NETs quantified by histone-elastase.

7.2.4. Statistical Analyses / Methods

Unadjusted means and standard errors will be calculated.

7.2.5. Endpoint / Variables

Change from baseline in peripheral blood neutrophil NET formation.

7.2.6. Summary Measure

Unadjusted mean and standard error will be calculated for the danirixin and placebo arms at baseline, day 7 and 14. Unadjusted mean and standard error will be calculated for the percent change from baseline danirixin and placebo arms at day 7 and 14

7.2.7. Population of Interest

The mITT population will be used.

7.2.8. Statistical Analyses / Methods

7.2.8.1. Statistical Methodology Specification

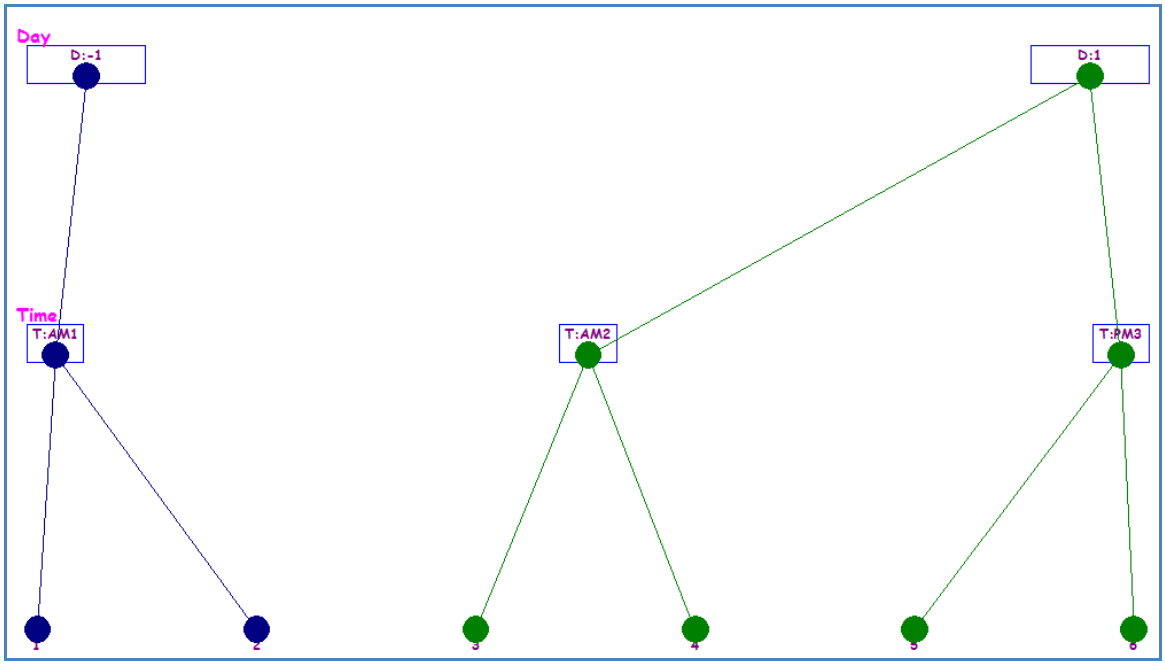
Unadjusted means and standard errors will be calculated.

7.3. Exploratory Efficacy Analyses

7.3.1. Endpoint / Variables

Exploratory endpoints include volatile organic compounds (VOC), ex-vivo neutrophil phagocytosis of bacteria by flow cytometry, and blood biomarkers. The blood biomarkers are plasma fibrinogen, serum C-reactive protein. Only VOCs from Cyranose, ex-vivo neutrophil phagocytosis and blood biomarkers will be part of SAC. No formal statistical analysis will be used to summarize the blood biomarkers, only unadjusted means. The urine will be stored for a two-year period, during which if there is a biomarker assay that comes forth that will support danirixin development program, analysis may be run.

The between tube, within day, and between day variability of the Cyaronose device will calculated using a multilevel multivariate model. Day will be the top level, followed by time of day, and tube. An unstructured covariance should be used to model the relationship between sensors, but the same covariance structure should be used across all tubes. Assume a constant variance between morning and afternoon and between days. Below is the model diagram for a single subject.



$$Y_{ijkl} = \mu + S_i + D_{i(j)} + T_{k(ij)} + \varepsilon_{ijkl}$$

In the case where the multilevel multivariate model does not converge then treat each sensor as independent and just run the multilevel model. If the multilevel models do not coverage, day and time of day can be collapsed into a single time level, in which we will only provide the variability of time rather than within day and between day.

Sputum microbiome, VOCs, and the relationship there in, will be investigated, but not included in the SAC due to the length of time needed to analysed the microbiome. The sputum microbiome will be analysed by Dundee. A secondary RAP to investigate VOCs and sputum microbiome will be written by the Computational Biology group to detail the analysis for this data. The results of this analysis will be written up in a report and added as an addendum to the CPSR.

8. SAFETY ANALYSES

The safety analyses will be based on the mITT population.

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 11: List of Data Displays.

8.2. Adverse Events of Special Interest Analyses

A comprehensive list of MedDRA terms based on clinical review will be used to identify each type of event. SRT, safety review team, has decided the Infective Pneumonia SMQ will used to identify AESI. The details of the planned displays are provided in Appendix 11: List of Data Displays.

8.3. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Haematology laboratory tests, Urinalysis, and liver function tests will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 11: List of Data Displays. The blood biomarkers, plasma fibrinogen and serum C-reactive protein, will be in the efficacy outputs.

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 11: List of Data Displays. Summaries of spirometry will also be created.

9. PHARMACOKINETIC ANALYSES

9.1. Primary Pharmacokinetic Analyses

9.1.1. Endpoint / Variables

9.1.1.1. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 12.5.3 Reporting Standards for Pharmacokinetic)

9.1.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis per 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 pharmacokinetic parameters listed below will be determined from the blood concentration-time data on Day 1 and Day 14, as data permits.

Parameter	Parameter Description
AUC(0-t)	Area under the concentration-time curve from time zero to the time of the last quantifiable concentration (C(t)) will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
Cmax*	Maximum observed concentration, determined directly from the concentration-time data.
tmax	Time to reach Cmax, determined directly from the concentration-time data.
tlast	Time of last quantifiable concentration

NOTES:

- Additional parameters may be included as required.

Unless otherwise specified, endpoints / variables defined in Section 9.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

10. POPULATION PHARMACOKINETIC (POPPK) ANALYSES

PK data from this study may be combined with historic data for the purposes of population PK modelling which would be the subject of a separate analysis plan and would be presented separately from the main clinical study report (CSR).

To support this analysis a PopPK dataset will be generated. The details for the dataset specifications are provided in Section 12.8 Appendix 9.

11. REFERENCES

GlaxoSmithKline Document Number 2017N314013_00, Protocol: Randomized double blind (sponsor unblind) study evaluating the effect of 14 days of treatment with danirixin (GSK1325756) on neutrophil extracellular traps (NETs) formation in participants with stable chronic obstructive pulmonary disease (COPD), 16 May 2017

12. APPENDICES

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

12.1.1. Exclusions from Per Protocol Population

No per protocol analysis is defined in this study.

12.2. Appendix 2: Schedule of Activities

12.2.1. Protocol Defined Schedule of Events

Table 1 Schedule of activities

Procedure	Pre-Screening and Screening[1]		Treatment Period (14 days)			Follow-up Phone call	Unscheduled visit [2]	Notes
	V0	V1	V2	V3	V 4	V5		
Day	Day -30 to -1		D 1	D 7	D14	D 21	As required	
Assessment window				±1d	±1d	± 3d	As required	
Written, informed consent	X							
Inclusion and exclusion criteria	X							Recheck clinical status before randomization.
Demography, Medical history	X							
Baseline COPD assessment test (CAT) score	X							
Adverse event (AE)/Serious adverse event (SAE) review	X	←==========			→	X	X	
Concomitant medication review	X	←==========			→	X	X	
Full physical examination including height and weight	X						X	
Vital signs	X	X	X	X	X		X	
Volatile organic compound (VOC) measurement	X[3]	X[3,4]	X[5]	X[3]	X[3]		X	
Spirometry	X		X		X		X	
Induced Sputum Samples (including biomarker samples)	X	X [4]	X	X	X		X	
Spirometry post-Sputum Induction	X	X [4]	X	X	X		X	
Triplicate 12-lead ECG		X	X		X		X	
Chest X-ray (historical within 1 year acceptable)		X						
HIV, Hepatitis B and C screening		X[6]						
Laboratory assessments (clinical chemistry including liver chemistries, haematology, biomarkers)		X	X		X		X	
Pharmacokinetic (PK) sample			X[7]	X[8]	X[7]		X	See footnotes for timings of PK sampling
Genetic sample			X[9]					Pre-dose (baseline) sample.
Urinary Pregnancy test (WOCBP only)		X[10]	X[10]		X[10]		X[10]	

Procedure	Pre-Screening and Screening[1]		Treatment Period (14 days)			Follow-up Phone call	Unscheduled visit [2]	Notes
	V0	V1	V2	V3	V 4	V5		
Urinalysis (including biomarker samples)		X	X		X		X	
Randomization			X					All baseline assessments at V2 should be completed prior to randomization
Study treatment			X	←→	X			
Dispense study medication			X					
Monitor IP compliance (via manual counting and App)			X	X	X			Digital App monitoring to begin at V2
Collect IP					X			

- The timing and number of planned study assessments, including safety, pharmacokinetic, pharmacodynamic/biomarker or other 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 IRB/IEC will be informed of any safety issues that require alteration of the safety monitoring scheme or amendment of the Informed consent form (ICF).
- Safety assessments should be performed in the following order where applicable/ possible: vital signs, ECG measurements, blood samples and spirometry.

1. Screening visit is split into pre-screening on visit 0 and screening on visit 1 although the visits may be performed on the same day. This is to a) enable participants to potentially have more than one attempt at sputum induction for meeting eligibility and b) to only collect minimal screening data for subjects who fail on the basis of the elevated NETs since that is the key inclusion criteria that may not be known from medical records.
2. Unscheduled visits may be used to collect information related to adverse events, for follow up of any safety assessments, and also to complete assessments where participants were not able to perform these within the visit window for any reason. It is not necessary to carry out all of the assessments listed under an unscheduled visit at a single visit; the assessments performed should be driven by the need for the visit.
3. VOC measurement should be undertaken prior to sputum induction at these visits.
4. Sputum induction (and associated VOC measurement and safety spirometry) at visit 1 is only necessary if participant unable to give sample at visit 0. Where the participant is judged by the investigator to have a borderline sputum NETs level (<0.5 units/ml) at visit 0, they will be invited to give a second sputum sample on visit 1 to re-assess eligibility.
5. VOC measurements should be undertaken at the following timepoints at this visits: prior to sputum induction,and 4 hours post dose
6. Hepatitis B (HBsAg) and Hepatitis C (HepC antibody) testing is required. If testing otherwise performed within 3 months prior to the first dose of study treatment, testing at screening is not required. Hepatitis C Ribonucleic acid (RNA) testing is optional; however a confirmatory negative Hepatitis C RNA test must be obtained, to be able to enroll participants with positive Hepatitis C antibody due to prior resolved disease.
7. At visits 2 and 4, PK samples should be collected at the following time-points: pre-dose, 0.5, 1, 2 and 4 hours post-dose.
8. At visit 3 only a pre-dose PK sample should be collected.
9. Agreeing to genetic sample consent is not required for overall study participation. Informed consent for genetic sample must be obtained prior to taking sample.
10. Pregnancy testing only required for women of child bearing potential (WOCBP). A positive urine pregnancy test requires confirmation with a serum pregnancy t

12.3. Appendix 3: Assessment Windows

12.3.1. Definitions of Assessment Windows for Analyses

Use nominal time of assessment.

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

12.4.1. Study Phases

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

Study Phase	Definition
Pre-Treatment	Date ≤ Study Treatment Start Date
On-Treatment	Study Treatment Start Date < Date ≤ Study Treatment Stop Date +1
Post-Treatment	Date > Study Treatment Stop Date +1

12.4.1.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is before date of start of treatment
Concomitant	Any medication that is not a prior

NOTES:

- Please refer to Appendix 7: Reporting Standards for Missing Data for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

12.4.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	• If AE onset date is on or after treatment start date & on or before treatment stop date. • Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date +1

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.

12.5. Appendix 5: Data Display Standards & Handling Conventions

12.5.1. Reporting Process

Software	
• The currently supported versions of SAS Studio 3.6 (Basic Edition) will be used.	
Reporting Area	
HARP Server	: \\UK1SALX00175.CORPNET2.com
HARP Compound	: \arprod\gsk1325756
Analysis Datasets	
• Analysis datasets will be created according to Legacy GSK A&R dataset standards.	
Generation of RTF Files	
• RTF files will be generated for final analysis outputs	

12.5.2. Reporting Standards

General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated (IDSL Standards Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics
• Do not include subject level listings or figures 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 or provided by vendor. • 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 NETs the individual data will be provided according to the appropriate level of precision for the 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 participant'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.	

12.5.3. 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 GUI_51487 and PKONE document. 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. Additionally, include geometric mean and 90% CI for the summary of blood concentration data
NONMEM/Pop PK File	Pop-PK file (CSV format) for the POP-PK analysis by Clinical Pharmacology Modelling and Simulation function will be created according to the data specification detailed in Appendix 9.
NONMEM/PK/PD File	Not applicable.
Pharmacokinetic Parameter Derivation	
PK Parameter to be Derived by Programmer	None.
Pharmacokinetic Parameter Data	
Is NQ impacted PK Parameters Rule Being Followed	No.
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards.

12.6. Appendix 6: Derived and Transformed Data

12.6.1. General

Multiple Measurements at One Analysis Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • If there are two values within a time window (as per Section 12.3.1) the value closest to the target day for that window will be used. If values are the same distance from the target, then the mean will be taken.   ○ For NETs: If there are unscheduled visits between screening and visit 2 use the last unscheduled visit prior to visit 2. • 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

12.6.2. Study Population

Treatment Compliance
• Treatment compliance will be calculated based on the formula: **Treatment Compliance = Number of Actual Doses / (Planned Treatment Duration in Days * Frequency)** • Frequency is 2 for BID Treatment compliance could be greater than 100% if there are events of overdose. • Planned Treatment Duration is defined as 14 days
Extent of Exposure
• Number of days of exposure to study drug will be calculated based on the formula: **Duration of Exposure in Days = Treatment Stop Date – (Treatment Start Date) + 1**
Age

• Age will be calculated based off the date participants signed consent forms
• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
  ○ Any participant with a missing day will have this imputed as day '15'.
  ○ Any participant with a missing date and month will have this imputed as '30th June'.
• Birth date will be presented in listings as 'YYYY'.

Smoking Status
• If the last smoked date (SUSMLSDT) is missing and a partial date (SUSMLSD) is not missing, then the following imputation should be applied to the partial smoking date for use in the reclassification of smoking status calculation: ○ '01' will be used for the day and 'Jan' will be used for the month.

Treatment Compliance
• Former smokers will be reclassified as current smokers if screening date – last smoked date < 183 days.

12.6.3. Efficacy

Change from Baseline
• Change from Baseline will be calculated based on the formula: **Change from Baseline = Value – Value on day 1** • Use the most recent pre-dose value for baseline. In the case where there is a bad sample on day 1 use screening •

12.6.4. Dataset to Protocol Mapping

Protocol Variable	BICAT (BIOMARK)	MITEST (MICROSCOPY)	MITSTD (MICROSCOPY)	SPECTYPE (MICROSCOPY)
Reduction in sputum NET area quantification by microscopy		AK005	26	C13278
Reduction in sputum NETs (quantified by Histone-elastase complexes)	HISTELAS			C13278
Reduction in sputum NETS (quantified by Deoxyribonucleic acid [DNA]-elastase complexes)	DNAELAS			C13278
Change from baseline in sputum resistin levels	RESIST			C13278
Change from baseline in the ratio of sputum NETs to sputum neutrophils		AW002		C13278
Change from baseline in sputum elastase activity	ELASTASE			C13278

Protocol Variable	BICAT (BIOMARK)	MITEST (MICROSCOPY)	MITSTD (MICROSCOPY)	SPECTYPE (MICROSCOPY)
Change from baseline in peripheral blood neutrophil NET formation (DNA release, microscopy)		AK005	8	C12434

12.7. Appendix 7: Reporting Standards for Missing Data

12.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion (i.e. as specified in the protocol) was defined as those who have completed the assessments supporting the primary endpoint • Withdrawn participants 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.

12.7.2. Handling of Missing Data

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

12.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant 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 4: 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. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing. • If treatment phase for an AE is missing due to missing dates class as on-treatment
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 recorded partial date will be displayed in listings.

12.8. Appendix 8: Values of Potential Clinical Importance

12.8.1. Laboratory Values

Hematology Analyte (units)	Effect	COPD Patients	
		Low	High
Platelet Count (x10^9/L)		0.90x	1.10x
Red Blood Cell Count (x10^{12}/L)		0.93x	1.07x
White Blood Cell Count (x10^9/L)		0.70x	1.60x
Hemoglobin (g/L)	Males	0.85x	1.20x
	Females	0.85x	1.20x
Hematocrit (Ratio of 1)	Males	0.50x	1.30x
	Females	0.50x	1.30x
MCV (fL)		0.25x	2.00x
MCH (pg)		0.85x	1.20x
Neutrophils (10^9/L)		<1.0	>10
Lymphocytes (10^9/L)		<1.2	>11.2
Monocytes (10^9/L)		<0.16	>2.6
Eosinophils (10^9/L)			>1.2
Basophils (10^9/L)			>0.85

Note: Multipliers are identified by "x", otherwise actual comparison values are provided with units.

Chemistry Analyte	Effect	COPD Patients	
		Low	High
BUN (mmol/L)		0.70x	1.60x
Creatinine (μmol/L)			1.30x (or >27 μmol/L increase from baseline)
Glucose (mmol/L)			1.20x
Sodium (mmol/L)		0.80x	1.15x
Potassium (mmol/L)		0.75x	1.30x
Calcium (mmol/L)	Males	0.85x	1.08x
	Females	<0.499 mmol/l	>1.7465 mmol/l
Total Protein (mg/dL)			1.25x

Note: Multipliers are identified by "x", otherwise actual comparison values are provided with units.

Liver Function Test Analyte	Effect	PCI Range	Unit
ALT/SGPT	High	≥ 3x ULN	U/L
AST/SGOT	High	≥ 3x ULN	U/L
Alkaline Phosphatase	High	≥ 2x ULN	U/L
Direct Bilirubin	High	≥ 1.5x ULN	μmol/L

12.8.2. ECG

ECG Parameter	PCI Range	Unit
Absolute QTc Interval (QTcB, QTcF)	<300 or >500	msec
QT Interval	<300 or >500	msec
PR Interval	<120 or >210	msec
QRS Interval	<70 or >125	msec
Heart Rate	<35 or >120	bpm

Values based on the mean of triplicate

12.8.3. Vital Signs

Vital Sign Parameter	PCI Range	Unit
Systolic Blood Pressure	<90 or >160	mmHg
Diastolic Blood Pressure	<40 or >110	mmHg
Heart Rate	<35 or >120	bpm
Respiration Rate	<8 or >30	breaths /min

12.9. Appendix 9: Population Pharmacokinetic (PopPK) Analyses

12.9.1. Population Pharmacokinetic (PopPK) Dataset Specification

12.9.1.1. Handling Missing Demographic and Covariate Data

Missing demographic and covariate data will not be imputed.

12.9.1.2. Handling Missing Dose Times

Missing dose time information will be handled on a case by case basis by imputing this information based on prior dosing times or based on recorded PK collection times. The details of these imputations will be described in the report.

12.9.1.3. Handling Missing Times of PK Samples

Missing times for PK will be handled on a case by case basis by imputing this information based on the dose time and/or times of other PK. The details of these imputations will be described in the report.

12.9.1.4. Handling of PK Data Below the Lower Limit of Quantification

Any PK data below the lower limit of quantification will be set to missing.

12.9.1.5. Dataset Specification

General description and rules:

- Missing or unknown values in covariates, if not to be imputed, will be assigned -99.
- The dataset is sorted by STUD, SUBJID, DATE, CTIM, EVID descending.
- The data items (columns) in the analysis-ready data file will be provided the same order as follows.
- Non-quantifiable (NQ) concentration values will be included as detailed for the CONC variable.
- Non-numerical concentration values (such as NS, NR, NA) will not be included.
- Placebo subjects will not be included.
- The dataset will be a comma delimited ASCII text file and will be named:
    - NM.*compound.study*.PK.v1.csv
    - Where “compound” is the compound name (e.g. GSK1234567) and “study” is the study number (e.g. 207551).

Variable	Label (Variable description)	Type	Units	Missing value	Codes/Derivation/Notes
ID	NONMEM subject identifier	Integer	None	Never	Sequential subject identifier across study after data is sorted by STUD, SUBJID, DATE, RTFD, EVID. Numbering to start at 1. To be entered in all rows for each subject.
STUDYID	Unique identifier for a study	Char	None	Never	207551 for all records
STUD	Study ID	Num	None	Never	207551 for all records
SUBJID	Subject identifier for study	Char	None	Never	Subject identifier, which must be unique within the study. The identification number of the subject as recorded on the CRF. Exclude placebo subjects. Include subjects who have received IP and have at least one measureable drug concentration. To be entered in all rows for each subject.
COUNTRY	Country	Char	None	Never	Country of the investigational site in which the subject participated in the trial; e.g. USA. To be entered in all rows for each subject.
SITEID	Unique identifier for a study site	Num	None	Never	e.g. PPD any lead zero should not be included. To be entered in all rows for each subject.
CONC	Drug Concentration	Num	ng/mL	*Never*	CONC=0 for PK_GSK1325756 records. No sample (NS), insufficient sample (IS) and no result (NR) records will be excluded from dataset. CONC='.' for PK_GSK1325756 records < LOQ (i.e. if drug conc is NQ).
LNCONC	Natural log of CONC column	Num	ng/mL	Never	Natural log of CONC column. If CONC=0, then LNCONC='.'.
LLQ	Lower Limit of quantification	Num	ng/mL	Never	LLQ=5 or from source data if different. To be entered in all rows for each

Variable	Label (Variable description)	Type	Units	Missing value	Codes/Derivation/Notes
					subject.
LNLLQ	Natural log of LLQ column	Num	ng/mL	Never	Natural log of LLQ column. If LLQ=0, then LNLLQ='.'.
MATRIX	Sample matrix	Num	None	Never	MATRIX=1 (blood).
MATRTEXT	Sample matrix text	Char	None	Never	Text corresponding to code for MATRIX. Enter 'Blood' for all rows.
LABL	Label describing the record	Char	None	Never	LABL explains the type of measurement for CONC for the current record. LABL=DOSE_GSK1325756 for dose record. LABL=PK_GSK1325756 for blood concentration record.
DATE	Date of Record	MM/DD/YYYY	None	Never	Date of record.
DATETIME	Date and time of record	MM/DD/YYYY HH:MM:SS	None	Never	Date and time of record.
DAY	Study day number of record	Num	None	Never	Day of study relative to first IP dose.
NDAY	Nominal day	Num	day	Never	Schedule visit day of study relative to first IP dose.
NOMT	Nominal time since FIRST IP dose	Num	h	Never	Nominal time of study relative to first IP dose. NOMT=0 for first dosing record only.
NOMTLD	Nominal time since LAST IP dose prior to sample	Num	h	Never	Nominal time of study relative to last IP dose prior to sample. NOMTLD=0 for dosing records.
RTFD	Relative time from FIRST IP dose to current sample time	Num	h	Never	Actual time from FIRST dose of IP.
RTLD	Relative time from LAST IP dose prior to sample	Num	h	Never	Actual time from last dose of IP prior to sample. When LABL=DOSE_GSK1325756, RTLD=0. For pre-dose PK sample on Day 7, RTLD is relative to the previous dose.
DOSE	Dose amount	Num	mg	Never	DOSE=35. To be entered in all rows for each subject.

Variable	Label (Variable description)	Type	Units	Missing value	Codes/Derivation/Notes
DRUG	Name of drug	Char	None	Never	DRUG=GSK1325756. To be entered in all rows for each subject.
REG	Dosing Regimen	Integer	None	Never	REG=2 for BD. To be entered in all rows for each subject.
REGTEXT	Subject dose regimen text	Char	None	Never	REGTXT=BD, text corresponding to code for REG. To be entered in all rows for each subject.
ROUT	Route of administration	Integer	None	Never	ROUT=1 for PO. To be entered in all rows for each subject.
ROUTTEXT	Subject route of administration text	Char	None	Never	ROUTTEXT=PO, text corresponding to code for ROUT. To be entered in all rows for each subject.
CMT	NONMEM Compartment code	Integer	None	Never	CMT=1 for DOSE_GSK1325756 records. CMT=2 for PK_GSK1325756 records.
EVID	NONMEM Event ID	Integer	None	Never	EVID=1 for LABL= DOSE_GSK1325756. EVID=0 for LABL= PK_GSK1325756.
AMT	NONMEM Amount of drug administered	Num	mg	Never	AMT=0 for LABL= PK_GSK1325756 records. AMT=35 for LABL= DOSE_GSK1325756 records.
II	NONMEM Inter-dose interval	Integer	h	Never	II=0 for LABL= PK_GSK1325756. II=12 for LABL= DOSE_GSK1325756, except II=0 for LABL= DOSE_GSK1325756 on Day 1 only.
SS	Steady-state data item	Integer	None	Never	SS=0 for LABL= PK_GSK1325756 records. SS=1 for LABL= DOSE_GSK1325756 records, except SS=0 for LABL= DOSE_GSK1325756 records on Day 1 only.
RATE	NONMEM Rate of drug infusion	Integer	None	Never	RATE=0 for LABL= PK_GSK1325756 records. RATE=-2 for LABL= DOSE_GSK1325756 records.

Variable	Label (Variable description)	Type	Units	Missing value	Codes/Derivation/Notes
MDV	NONMEM Missing data value	Integer	None	Never	MDV=1 for LABL= DOSE_GSK1325756 records. MDV=0 for LABL= PK_GSK1325756 records. MDV=1 for LABL= PK_GSK1325756 records < LOQ (NQ).
VIS	Visit number	Integer	None	Never	From source data.
POP	Population	Integer	None	Never	POP=1, for COPD. To be entered in all rows for each subject.
POPTEXT	Subject population text	Char	None	Never	POPTEXT=COPD, text corresponding to code for POP. To be entered in all rows for each subject.
COH	Cohort	Integer	None	Never	COH=1. To be entered in all rows for each subject.
AGE	Subject Age	Integer	year	If missing impute with -99	From source data. To be entered in all rows for each subject.
SEX	Subject gender	Integer	None	Never	0=Male, 1=Female To be entered in all rows for each subject.
SEXTEXT	Subject gender text	Char	None	Never	Text corresponding to code for SEX, e.g. MALE or FEMALE). To be entered in all rows for each subject.
BMI	Baseline Body Mass Index	Num	kg/m^2	If missing impute with -99	Ensure consistent with S&P formula. E.g. Formula: Weight(kg)/(height(m)**2) To be entered in all rows for each subject.
BSA	Baseline Body Surface Area	Num	m^2	If missing impute with -99	Formula: BSA (m^2) = 0.024265 • Height(cm)$^{0.3964}$ • Weight(kg)$^{0.5378}$ Ensure consistent to with S&P formula. To be entered in all rows for each subject.
WT	Baseline Subject weight	Num	kg	If missing impute with -99	From source data. To be entered in all rows for each subject.
HT	Baseline Subject height	Num	m	If missing impute with -99	From source data. To be entered in all rows for each subject.
RACE1	Subject race code1	Integer	None	Never	From source data e.g. 1=African American / African

Variable	Label (Variable description)	Type	Units	Missing value	Codes/Derivation/Notes
					Heritage 2=American Indian or Alaska Native 3=Asian – Central / South Asian Heritage 4=Asian – East Asian Heritage 5=Asian – Japanese Heritage 6=Asian – South East Asian Heritage 7=Asian – Mixed Race 8=Native Hawaiian or other Pacific Islander 9=White – Arabic / North African Heritage 10=White – White / Caucasian / European Heritage 11=White – Mixed Race 12=Mixed Race To be entered in all rows for each subject.
RACE1TXT	Subject race text	Char	None	Never	Text corresponding to code for RACE1 To be entered in all rows for each subject.
RACE2	Subject race code2	Integer	None	Never	1=East Asian: Asian – East Asian Heritage & Asian – Japanese Heritage 2=White: White – Arabic / North African Heritage White – White / Caucasian / European Heritage 3=African: African American / African Heritage; 4=Other: American Indian or Alaska Native; Asian – Central / South Asian Heritage; Asian – South East Asian Heritage; Asian – Mixed Race; Native Hawaiian or other Pacific Islander; White – Mixed Race & Mixed Race To be entered in all rows for each subject.
RACE2TXT	Subject race text	Char	None	Never	Text corresponding to code for RACE2 To be entered in all rows for each subject.
ETHN	Subject ethnicity	Num	None	Never	From source data definition. E.g 1=Hispanic or Latino, 2=Non-

Variable	Label (Variable description)	Type	Units	Missing value	Codes/Derivation/Notes
					Hispanic To be entered in all rows for each subject.
ETHNTEXT	Subject ethnicity text	Char	None	Never	Text corresponding to code for ETHN. To be entered in all rows for each subject.
REGN	Region for subject	Num	None	Never	1 = East Asia (to include Japan, South Korea and Taiwan) 2 = Rest of the World (to include all other countries) To be entered in all rows for each subject.
SMOK	Subject smoking status	Integer	None	Never	0=Non-smoker, 1=Smoker, 2=Former smoker To be entered in all rows for each subject. Smoking status at baseline.
SMOKTEXT	Subject smoking status text	Char	None	Never	Text corresponding to code for SMOK. To be entered in all rows for each subject.
CMED1	Identifier for on-treatment COPD concomitant medication	Num	None	Never	0 = no concomitant use 1 = intermittent use 2 = continuous use To be entered in all rows for each subject.
CMED1TEXT	Subject CMED1 text	Char	None	Never	Text corresponding to code for CMED1. To be entered in all rows for each subject.
CRCL	Baseline Creatinine Clearance	Num	mL/min	If missing impute with -99	From source data. OR Specify appropriate formula e.g. Creatinine Clearance will be calculated based on the Cockcroft-Gault equation. • CrCL (ml/min) = [140 – AGE (in years)]*Weight(kg)*0.85 (for female patients) / [72* Serum Creatinine (micromol/L) * 0.0113 • Delete one as appropriate and ensure consistency with S&P

Variable	Label (Variable description)	Type	Units	Missing value	Codes/Derivation/Notes
					formula • To be entered in all rows for each subject.
CMED2	Identifier for on-treatment gastric acid reducing concomitant medication	Num	None	Never	0 = no concomitant use 1 = intermittent use 2 = continuous use To be entered in all rows for each subject.
CMED2TEXT	Subject concomitant medication text	Char	None	Never	Text corresponding to code for CMED2. To be entered in all rows for each subject.
CMED3	Identifier for on-treatment gastric acid increasing concomitant medication	Num	None	Never	0 = no concomitant use 1 = intermittent use 2 = continuous use To be entered in all rows for each subject.
CMED3TEXT	Subject concomitant medication text	Char	None	Never	Text corresponding to code for CMED3. To be entered in all rows for each subject.
CMED4	Identifier for on-treatment p-gp inhibitor concomitant medication	Num	None	Never	0 = no concomitant use 1 = intermittent use 2 = continuous use To be entered in all rows for each subject.
CMED4TEXT	Subject CMED4 text	Char	None	Never	Text corresponding to code for CMED4. To be entered in all rows for each subject.
CMED5	Identifier for on-treatment p-gp inducer concomitant medication	Num	None	Never	0 = no concomitant use 1 = intermittent use 2 = continuous use To be entered in all rows for each subject.
CMED5TEXT	Subject concomitant medication text	Char	None	Never	Text corresponding to code for CMED5. To be entered in all rows for each subject.
TBIL	Baseline Total bilirubin	Num	Specify	If missing impute with -99	Baseline defined in the source dataset To be entered in all rows for each subject.
TFIB	Baseline Fibrinogen	Num	Specify	If missing impute	Baseline defined in the source dataset

Variable	Label (Variable description)	Type	Units	Missing value	Codes/Derivation/Notes
				with -99	To be entered in all rows for each subject.

Current Therapies for COPD: CMED1

Long-acting β_2-agonists (LABAs)		
Formoterol Indacaterol Salmeterol Olodaterol		
Long acting anti-muscarinic antagonists (LAMAs)		
Tiotropium Aclidinium Bromide Glycopyrronium bromide Umeclidinium		
Long acting combination bronchodilators		
Albuterol/ipratropium bromide Vilanterol/umeclidinium Olodaterol/tiotropium Indacaterol/glycopyrrolate Formoterol/glycopyrrolate Formoterol/aclidinium		
Methylxanthines		
Theophylline Aminophylline	Bronchodilator effects and claimed anti-inflammatory effects.	Dose-related toxicity including the development of atrial and ventricular arrhythmias and grand mal seizures.
Inhaled glucocorticosteroids		
Beclomethasone Budesonide Fluticasone propionate Fluticasone furoate Mometasone		

Inhaled glucocorticosteroids (ICS, in combination with inhaled bronchodilators)		
Formoterol/budesonide Salmeterol/Fluticasone propionate Vilanterol/Fluticasone Furoate Formoterol/beclomethasone Formoterol/mometasone		
Inhaled glucocorticosteroids (ICS, in combination with inhaled LABA and LAMA)		
Fluticasone Furoate/Umeclidium/Vilanterol		
Phospodiesterase-4 inhibitors		
Roflumilast		
Antibiotics		
Macrolides (e.g. azithromycin, erythromycin)		

CMED2: Gastric acid reducing conmeds

Obs	VAR1	VAR2
1	Term Name	Code
2	ESOMEPRAZOLE MAGNESIUM	1479302
3	PEPTAZOL (NOS)	59841501
4	DOMPERIDONE MALEATE + RABEPRAZOLE SODIUM	54702201
5	CLARITHROMYCIN + LANSOPRAZOLE	54953101
6	PANTOPRAZOLE	1263201
7	ESOMEPRAZOLE	1479301
8	DOMPERIDONE + PANTOPRAZOLE	53545101
9	ZEGERID (NOS)	54613401
10	LANSOPRAZOLE SODIUM	1159002
11	ESOMEPRAZOLE STRONTIUM	1479304
12	ESOGARD (NOS)	59864501
13	OMEPRAZOLE MAGNESIUM	661203
14	ZOLTUM (NOS)	59177101
15	TENATOPRAZOLE	1401301
16	PRAZOL (NOS)	51163801
17	DEXLANSOPRAZOLE	53869001
18	DOMPERIDONE + RABEPRAZOLE	53611501
19	DOMPERIDONE + OMEPRAZOLE	53773301
20	CLARITHROMYCIN + LANSOPRAZOLE + TINIDAZOLE	53235701
21	LEVOSULPIRIDE + RABEPRAZOLE SODIUM	54347301
22	LEVOSULPIRIDE + RABEPRAZOLE	54342301
23	PROTON PUMP INHIBITOR NOS	53027601
24	IPP (NOS)	54019901
25	OMEPRAZOLE SODIUM	661202
26	PANTOPRAZOLE MAGNESIUM	1263203
27	ESOMEPRAZOLE SODIUM	1479303
28	DOMPERIDONE MALEATE + PANTOPRAZOLE SODIUM	54543201
29	PROTONIX (NOS)	54411301
30	GASTROZOL (NOS)	54724001
31	OMEPRAZOLE + SODIUM BICARBONATE	53827801
32	ALIMENTARY TRACT AND METABOLISM;DRUGS FOR	A02BC
33	LANSOPRAZOLE	1159001
34	MOSAPRIDE CITRATE + RABEPRAZOLE SODIUM	54691301
35	ESOMEPRAZOLE POTASSIUM	1479305

NDAY: For deriving the nominal day which is the planned day, DAY specific information is not available in EXPOSURE dataset. VISIT variable and the time and events table might have to be taken into account to find the exact plan of events.

NOMT: It is twice daily dosing with inter-dose interval given to be 12 hours. Therefore, to find the planned time of event since the first dose in hours, again the VISIT variable and time and events will have to be considered.

NOMTLD: In case of PK_GSK1325756 records, the planned time point variable will give the value of this variable for all the post-dose records. For the pre-dose records, this variable will have missing values since there is no fixed time point since the previous dose for pre-dose records.

RTFD: The time difference between the first dose of the subject and the current dose (when LABL=DOSE_GSK1325756) should be calculated in hours. The time difference

between the first dose of the subject and the PK sample collection time (when LABL=PK_GSK1325756) should be calculated in hours.

RTLD: The latest dose prior to the PK sample collection time will have to be found out and the time difference between that dose and the PK sample collection time will be calculated in hours.

12.10. Appendix 10: Abbreviations & Trade Marks

12.10.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
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
mITT	Modified Intent to Treat
NETs	Neutrophil Extracellular Traps
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
PopPK	Population PK
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RAMOS	Randomization & Medication Ordering System

Abbreviation	Description
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

12.10.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
None

Trademarks not owned by the GlaxoSmithKline Group of Companies
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12.11. Appendix 11: List of Data Displays

12.11.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.21	
Efficacy	2.1 to 2.22	2.1 to 2.18
Safety	3.1 to 3.14	
Pharmacokinetic	4.1 to 4.2	4.1 to 4.6
Section	**Listings**	
ICH Listings	1 to 30	
Other Listings	31 to 44	

12.11.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced by the name of the table or figure and if required example mock-up displays provided in Appendix 12: Example Mock Shells for Data Displays.

12.11.3. Deliverables

Delivery [Priority] [1]	Description
SAC [X]	Final Statistical Analysis Complete
D	Will be part of the abbreviated dry run

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

12.11.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	mITT	ES1	Summary of Subject Disposition for the Subject Conclusion Record	ICH E3, FDAAA, EudraCT, Use latest screening	SAC [2]
1.2.	mITT	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment	ICH E3	SAC [2]
1.3.	Enrolled	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements, Use latest screening. If a subject is rescreened only use final re-screen	SAC [2]
1.4.	Enrolled	NS1	Summary of Number of Subject by Country and Site ID	EudraCT/Clinical Operations	SAC [2]
1.5.	mITT	NS1	Summary of Number of Subject by Country and Site ID	EudraCT/Clinical Operations	SAC [2]
1.6.	Primary Completer	NS1	Summary of Number of Subject by Country and Site ID	EudraCT/Clinical Operations. If the primary completer and mITT population are the same do not recreate	SAC [2]
Protocol Deviation					
1.7.	mITT	DV1	Summary of Important Protocol Deviations	ICH E3	SAC [2]
1.8.	Enrolled	IE1	Summary of Inclusion/Exclusion Criteria Deviations for Screen or Run-in failures		SAC [2]
1.9.	mITT	IE1	Summary of Inclusion/Exclusion Criteria Deviations for the Modified Intent-to-treat Population		SAC [2]

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Population Analysed					
1.10.	Enrolled	SP1	Summary of Study Populations	IDSL Number of participants who were in the Enrolled population, who were randomized, the number in the mITT population. Of those in the mITT, the number and percentage of participants in the primary completer population	SAC [2]
Demographic and Baseline Characteristics					
1.11.	mITT	DM1	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	SAC [2]
1.12.	Primary Completer	DM1	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	SAC [2]
1.13.	Enrolled	DM11	Summary of Age Ranges	EudraCT	SAC [2]
1.14.	mITT	PD4	Summary of Screening and Baseline Spirometry Measures	Pre-BD FEV1 (L), Post-BD FEV1 (L), Predicted normal FEV1 (L), Percent predicted normal post-BD FEV1 (%), Percent predicted normal post-BD FEV1: <50%, >=50%, Post-BD FVC (L), Post-BD FEV1/FVC Footnote: Subjects are only supposed to have a Post Sputum Induction FEV1 at baseline if participant was unable to give a sample at Pre-Screening. The pre-screening and screening samples for this measure are combined.	SAC [2]
1.15.	mITT	SU1	Summary of Smoking History and Smoking Status at Screening	Include smoking status, smoking pack years, cigarettes smoked/day	SAC [2]
1.16.	mITT	DM6	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT	SAC [2]

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Prior and Concomitant Medications					
1.17.	mITT	MH4	Summary of Current Medical Conditions	ICH E3	SAC [2]
1.18.	mITT	MH4	Summary of Past Medical Conditions	ICH E3	SAC [2]
1.19.	mITT	CM1	Summary of Concomitant Medications	ICH E3	SAC [2]
1.20.	mITT	CM1	Summary of COPD Concomitant Medications Taken Pre-treatment		SAC [2]
1.21.	mITT	CM1	Summary of COPD Concomitant Medications Taken Post-treatment		SAC [2]

12.11.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
NETs					
2.1	Primary Completer		Summary of Adjusted Mean Change from Baseline of NETs Quantified by Histone-Elastase		D, SAC [2]
2.2	Primary Completer		Summary of Unadjusted Means of NETs	Histone, DNA, and microscopy quantified	D, SAC [1]
2.3	Modified Primary Completer		Summary of Unadjusted Means of NETs for the Modified Primary Population	Histone, DNA, and microscopy quantified. This population will only be use if this increases the available sample from the Primary completer population by 20%.	SAC [2]
2.4	Primary Completer		Summary Unadjusted Mean Change from Baseline of NETs	Include percent change from baseline	D, SAC [2]
2.5	Primary Completer		Summary of the Ratio of Sputum NETs to Sputum Neutrophils		D, SAC [2]
2.6	Primary Completer		Summary of Change from Baseline in the Ratio of Sputum NETs to Sputum Neutrophils		D, SAC [2]
2.7	Primary Completer		Summary of Sputum Neutrophils		D, SAC [1]
2.8	Primary Completer		Summary of Change from Baseline in Sputum Neutrophils		D, SAC [2]
2.9	mITT		Summary of Peripheral Blood Neutrophil NETs Formation	Will be measured by DNA release and microscopy, summarise no PMA and PMA values septately, but include both on the table. Only collected at baseline and day 14	D, SAC [1]

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.10	mITT		Summary of Change from Baseline in Peripheral Blood Neutrophil NETs Formation	Will be measured by DNA release and Microscopy	D, SAC [2]
2.11	mITT		Summary of Sputum Quality	Number of subjects with Insufficient Tissue, Poor Quality, Acceptable, and Good Quality samples see MISPQL variable for quality flag Mean and SD of Squamous epithelial cells. Mean and SD of Viable Leukocytes.	D, SAC [2]
2.12	Primary Completer		Summary of Sputum Quality	Number of subjects with Insufficient Tissue, Poor Quality, Acceptable, and Good Quality samples see MISPQL variable for quality flag Mean and SD of Squamous epithelial cells. Mean and SD of Viable Leukocytes .	D, SAC [2]
CAT					
2.13	mITT		Summary of Baseline CAT		SAC [2]
Biomarker					
2.14	Primary Completer		Summary of Change from Baseline Sputum Resistin Levels		D, SAC [2]
2.15	Primary Completer		Summary of Sputum Resistin Levels		D, SAC [2]
2.16	Primary Completer		Summary of Change from Baseline in Sputum Elastase Activity		D, SAC [2]
2.17	Primary Completer		Summary of Sputum Elastase Activity		D, SAC [2]

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.18	mITT		Summary of Change from Baseline in Ex-Vivo Neutrophil Phagocytosis of Bacteria by Flow Cytometry		D, SAC [2]
2.19	mITT		Summary of Ex-Vivo Neutrophil Phagocytosis of Bacteria by Flow Cytometry		D, SAC [2]
2.20	mITT		Summary of Change from Baseline of Blood Biomarkers	Include plasma fibrinogen and serum C-reactive protein. For values below the LLQ use X/2	D, SAC [2]
2.21	mITT		Summary of Blood Biomarkers	Include plasma fibrinogen and serum C-reactive protein. For values below the LLQ use X/2	D, SAC [2]
Exploratory					
2.22	mITT		Summary of VOCs Variablity		SAC [2]

12.11.6. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
NETs					
2.1	Primary Completer		Adjusted Mean (95% CI) Change from Baseline of NETs Quantified by Histone-Elastase		D, SAC [2]
2.2	Primary Completer		Unadjusted Mean and (95% CI) Change from Baseline of NETs Quantified by Histone-Elastase, DNA-Elastase, and Microscopy	Please add text below indicating the number of subjects in each quality category. Percentage change.	D, SAC [2]

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.3	Modified Primary Completer		Unadjusted Mean and (95% CI) Change from Baseline of NETs Quantified by Histone-Elastase, DNA-Elastase, and Microscopy for the Modified Primary Population	Please add text below indicating the number of subjects in each quality category. Percentage change. This population will only be use if this increases the available sample from the Primary completer population by 20%.	SAC [2]
2.4	Primary Completer		Spaghetti Plot of Change from Baseline of NETs		D, SAC [2]
2.5	Primary Completer		Spaghetti Plot of NETs		D, SAC [2]
2.6	Modified Primary Completer		Spaghetti Plot of NETs for the Modified Primary Population	This population will only be use if this increases the available sample from the Primary completer population by 20%.	SAC [2]
2.7	Primary Completers		Spaghetti and Boxplot of Baseline and Day 14 of NETs Quantified by Histone Elastase		D, SAC [2]
2.8	Primary Completers		Spaghetti and Boxplot of Baseline and Day 14 of Neutrophils		D, SAC [2]
2.9	mITT		Spaghetti and Boxplot of Baseline and Day 14 of Peripheral Blood NETs	For no PMA values only. Will be measured by DNA release and microscopy	D, SAC [2]
2.10	Primary Completer		Spaghetti Plot of Change from Baseline in the Ratio of Sputum NETs to Sputum Neutrophils		D, SAC [2]
2.11	Primary Completer		Spaghetti Plot of Ratio of Sputum NETs to Sputum Neutrophils		D, SAC [2]

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.12	mITT		Spaghetti Plot of Change from PMA in Peripheral Blood Neutrophil NETs Formation	Facet the plot by the change that occurs on day -1 and on day 14. Will be measure by DNA release and microscopy	D, SAC [2]
2.13	mITT		Spaghetti and Boxplot of Peripheral Blood Neutrophil NETs Formation		D, SAC [2]
2.14	mITT		Boxplot of Change from Baseline in Peripheral Blood Neutrophil NETs Formation	For Placebo and treatment	D, SAC [2]
2.15	Primary Completer		Spaghetti Plot of Change from Baseline of Sputum Neutrophils		D, SAC [2]
2.16	Primary Completer		Spaghetti Plot of Sputum Neutrophils		D, SAC [2]
Biomarkers					
2.17	mITT		Mean and (95% CI) of Change from Baseline in Ex-Vivo Neutrophil Phagocytosis of Bacteria by Flow Cytometry		SAC [2]
2.18	mITT		Mean and (95% CI) of Change from Baseline of Blood Biomarkers		SAC [2]

12.11.7. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	mITT	AE1CP	Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3	SAC [2]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.2.	mITT	AE1	Summary of Adverse Events of Special Interest	the specific events of interest will be based on the safety review team (SRT) agreements in place at the time of reporting	SAC [2]
3.3.	mITT	AE1CP	Summary All Drug-Related Adverse Events by System Organ Class and Preferred Term	ICH E3	SAC [2]
3.4.	mITT	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and Occurrences)	FDAAA, EudraCT	SAC [2]
Serious and Other Significant Adverse Events					
3.5.	mITT		Summary of Change from Baseline of Spirometry		SAC [2]
3.6.	mITT		Summary of Spirometry		SAC [2]
3.7.	mITT	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences)	FDAAA, EudraCT	SAC [2]
Laboratory: Chemistry					
3.8.	mITT	LB1	Summary of Chemistry Changes from Baseline	ICH E3	SAC [2]
Laboratory: Hematology					
3.9.	mITT	LB1	Summary of Hematology Changes from Baseline	ICH E3	SAC [2]
Laboratory: Urinalysis					
3.10.	mITT	LB1	Summary of Urine Concentration Changes from Baseline	ICH E3	SAC [2]
Laboratory: Hepatobiliary (Liver)					
3.11.	mITT	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting	IDSL	SAC [2]
ECG					
3.12.	mITT	EG1	Summary of ECG Findings	IDSL	SAC [2]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.13.	mITT	EG2	Summary of Change from Baseline in ECG Values by Visit	IDSL	SAC [2]
Vital Signs					
3.14.	mITT	VS1	Summary of Change from Baseline in Vital Signs	ICH E3	SAC [2]

12.11.8. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Whole Blood Pk					
4.1.	PK	PKCT1	Summary of Danirixin Whole Blood Pharmacokinetic Concentration-Time Data		SAC[2]
4.2.	PK	PKPT4	Summary of Derived Danirixin Whole Blood Pharmacokinetic Parameters		SAC[2]

12.11.9. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.1.	PK	PKCF1p	Individual Whole Blood Danirixin Concentration-Time Plots by Subject (Linear and Semi-log)	1. X-axis displays actual relative time 2. Include line for LLQ along with footnote defining LLQ value 3. Include values below LLQ 4. Overlay Day 1 and 14	SAC [2]
4.2.	PK	PKCF6	Individual Whole Blood Danirixin Concentration-Time Plots by Day (Linear and Semi-log)	1. X-axis displays actual relative time 2. Include line for LLQ along with footnote defining LLQ value 3. Include values below LLQ	SAC [2]
4.3.	PK	PKCF4	Mean (±SD) Whole Blood Danirixin Concentration-Time Plots (Linear and Semi-log)	1. Include the full SD bars at each time point 2. X-axis displays planned relative time 3. Include line for LLQ along with footnote defining LLQ value	SAC [2]
4.4.	PK	PKCF5	Median (Range) Whole Blood Danirixin Concentration-Time Plots (Linear and Semi-log)	1. Include bars for range at each time point 2. X-axis displays planned relative time 3. Include like for LLQ along with footnote defining LLQ value	SAC [2]

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.5.	PK		Scatter plot of Efficacy versus Danirixin Concentration (Trough)	Spumtum Neutrophil Count and Peripheral Blood Neutrophil Count Include Placebo imputed as DNX conc=0ng/mL, include DNX conc=NQ imputed as LLOQ/2, where LLOQ=5ng/mL By Day	SAC [2]
4.6.	PK		Scatter plot of Safety versus Danirixin Concentration (Trough)	C-reactive Protein (CRP) Include Placebo imputed as DNX conc=0ng/mL, include DNX conc=NQ imputed as LLOQ/2, where LLOQ=5ng/mL By Day	SAC [2]

12.11.10. 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]
2.	Enrolled	ES2	Listing of Reasons for Study Withdrawal	ICH E3	SAC [2]
3.	mITT	SD2	Listing of Reasons for Study Treatment Discontinuation	ICH E3	SAC [2]
4.	mITT	BL1	Listing of Subjects for Whom the Treatment Blind was Broken	ICH E3	SAC [2]
5.	mITT	TA1	Listing of Planned and Actual Treatments	IDSL	SAC [2]
Protocol Deviations					
6.	mITT	DV2	Listing of Important Protocol Deviations	ICH E3	SAC [2]
7.	mITT	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3, Add a flag if subject got randomized and dosed	SAC [2]
Populations Analysed					
8.	Enrolled	SP3	Listing of Participants Excluded from Any Population	ICH E3	SAC [2]
Demographic and Baseline Characteristics					
9.	mITT	DM2	Listing of Demographic Characteristics	ICH E3	SAC [2]
10.	mITT	DM9	Listing of Race	ICH E3	SAC [2]
11.	mITT		Listing of Change in Smoking Status from Screening		SAC [2]
Prior and Concomitant Medications					
12.	mITT	CP_CM3	Listing of Concomitant Medications	IDSL	SAC [2]
Exposure and Treatment Compliance					
13.	mITT	EX3	Listing of Exposure Data	ICH E3	SAC [2]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
14.	mITT	AE8CP	Listing of All Adverse Events	ICH E3	SAC [2]
15.	mITT	AE8CP	Listing of Adverse Events of Special Interest	ICH E3	SAC [2]
16.	Enrolled	AE8CP	Listing of All Adverse Events for Subject not in mITT	ICH E3	SAC [2]
17.	mITT	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	SAC [2]
18.	mITT	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	SAC [2]
Serious and Other Significant Adverse Events					
19.	mITT	AE7	Listing of Adverse Event of Special Interest	the specific events of interest will be based on the safety review team (SRT) agreements in place at the time of reporting	SAC [2]
20.	mITT	AE8CPa	Listing of Fatal Serious Adverse Events	ICH E3	SAC [2]
21.	mITT	AE8CPa	Listing of Non-Fatal Serious Adverse Events	ICH E3	SAC [2]
22.	mITT	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	SAC [2]
23.	mITT	AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	SAC [2]
Hepatobiliary (Liver)					
24.	mITT	MH2	Listing of Medical Conditions for Subjects with Liver Stopping Events	IDSL	SAC [2]
25.	mITT	SU2	Listing of Substance Use for Subjects with Liver Stopping Events	IDSL	SAC [2]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
All Laboratory					
26.	mITT	LB5	Listing of All Laboratory Data for Subjects with Any Value of Potential Clinical Importance	ICH E3	SAC [2]
27.	mITT	LB5 / LB6	Listing of Laboratory Values	IDSL	SAC [2]
28.	mITT	UR2A	Listing of Urinalysis Data for Subjects with Any Value of Potential Clinical Importance	ICH E3, Use IDSL standard range	SAC [2]
ECG					
29.	mITT	EG3 / EG4	Listing of ECG Values	IDSL	SAC [2]
Vital Signs					
30.	mITT	VS4 / VS5	Listing of Vital Signs	IDSL	SAC [2]

12.11.11. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
NETs					
31.	Primary Completer		Listing of NETs	Include Change from Baseline	SAC [2]
32.	Primary Completer		Listing of the Ratio of Sputum NETs to Sputum Neutrophils	Include Change from Baseline	SAC [2]
33.	mITT		Listing of Peripheral Blood Neutrophil NETs Formation	Include Change from Baseline	SAC [2]
34.	Primary Completer		Listing of Sputum Quality Measures	Quality measure, viability of leukocytes, and Squamous epithelial cells	SAC [2]
Spirometry					
35.	mITT		Listing of Spirometry	Include Change from Baseline	SAC [2]
36.	mITT		Listing of Baseline CAT	Flag to indicate if they are part of the primary completer population	SAC [2]
Exploratory					
37.	mITT		Listing of Treatment Adherence		SAC [2]
38.	mITT		Listing of VOCs		SAC [2]
Biomarker					
39.	Primary Completer		Listing of Sputum Resistin	Include Change from Baseline	SAC [2]
40.	Primary Completer		Listing of Sputum Elastase	Include Change from Baseline	SAC [2]
41.	mITT		Listing of Ex-Vivo Neutrophil Phagocytosis of Bacteria by Flow Cytometry	Include Change from Baseline	SAC [2]

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
42.	mITT		Listing of Blood Biomarkers	Include plasma fibrinogen and serum C-reactive protein. Include Change from Baseline	SAC [2]
PK					
43.	PK	PKCL1P	Listing of Danirixin Whole Blood Pharmacokinetic Concentration-Time Data		SAC [2]
44.	PK	PKPL1P	Listing of Derived Danirixin Whole Blood Pharmacokinetic Parameters		SAC [2]

12.12. Appendix 12: Example Mock Shells for Data Displays

Available Upon Request