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

Title	:	Reporting and Analysis Plan for Study 205864: A randomized, double-blind, sponsor open, placebo-controlled, 52-week study evaluating the effect of danirixin (GSK1325756) on lung function and health related quality of life in participants with mild to moderate Chronic Obstructive Pulmonary Disease (COPD)
Compound Number	:	GSK1325756
Effective Date	:	25-MAR-2019

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report (CSR) for Protocol 205864.
- This RAP is intended to describe the planned efficacy and safety 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):

PPD Study Statistician (Clinical Statistics)	25-MAR-2019

RAP Team Review Confirmation

(Method: E-mail)

Reviewer	Date	Approval Method
PPD CIL (Respiratory TAU)	19-MAR-2019	E-mail response
PPD Programmer (Clinical Programming)	25-MAR-2019	E-mail response

Clinical Statistics & Programming Line Approvals

(Method: Pharma TMF eSignature)

Approver	Date	Approval Method
PPD Project Statistician (Respiratory Clinical Statistics) On behalf of PPD Line Manager (Respiratory Clinical Statistics)	20-MAR-2019	eTMF e-Signature
PPD Manager Programming (Respiratory Clinical Programming)	21-MAR-2019	eTMF e-Signature

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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 Synoptic Clinical Study Report for Protocol of study 205864 (GSK Document No 2016N293064_3)

Revision Chronology:		
2016N293064	21-MAR-2017	Original
2016N293064_01	17-MAY2017	Excludes the enrolment of women of childbearing potential
2016N293064_02	24-JUL-2017	Removal of requirement for male contraception with partners of WOCBP. Addition of mobile spirometer (MicroDiary) as a medical device
2016N293064_03	18-MAY-2018	Updated to reflect that cohorts in addition to COPDGene may be used to support recruitment. Removed the use of the Random Forest data in patient selection and changed history of lung function decline from 20mL/yr to 15 mL/yr. Changed inclusion criteria from weight >45kg to body mass index ≥ 21.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Changes from the originally planned statistical analysis specified in the protocol are outlined in Table 1.

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	**Reporting & Analysis Plan**	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
• All Participants population	• All Subjects population	• R&D Clinical Data Standards Board (CDSB) recommendation to use the term 'Subjects' in all displays (Tables, Figures & Listings)
• Random coefficients model analysis of rate of decline in FEV_1	• Summary Statistics	• Early study termination
• MMRM analysis of change from baseline of SGRQ-C and SGRQ-C domains	• Summary Statistics	• Early study termination
• SGRQ Responder analysis	• No analysis	• Early study termination
• Time to first HCRU COPD exacerbation	• No analysis	• Early study termination
• Study Population and Efficacy deliverables on ITT Population	• Change population of Study Population and Efficacy deliverables from ITT to	• Consistency among danirixin project

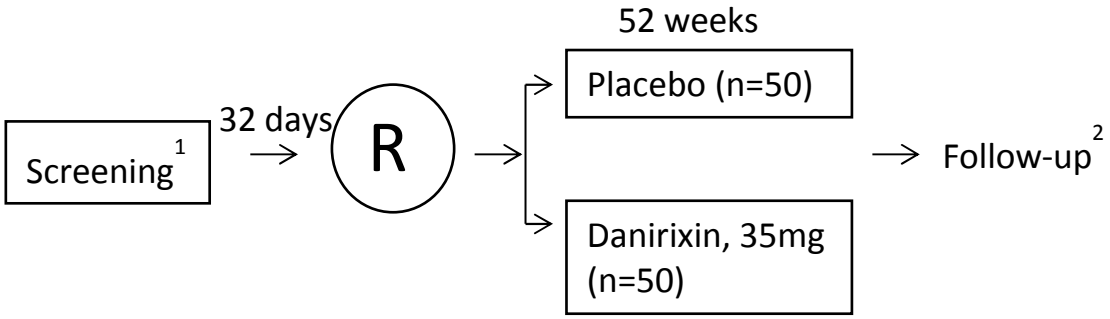
Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
	Safety population	• Primary interest on safety results Study Population and Efficacy tables should be a reflection of the focus
• Per protocol population	• Removal of per protocol population	• No analysis using per protocol population

2.2. Study Objectives and Endpoints

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To assess whether danirixin HBr 35mg tablets impact disease progression compared with placebo	• Rate of decline in FEV_1 (post-bronchodilator) • Change from baseline in St. George's Respiratory Questionnaire (SGRQ) total score (derived from SGRQ-C) at the end of the 52-week treatment period
Secondary Objectives	**Secondary Endpoints**
• To further characterize the safety of danirixin HBr 35mg compared to placebo in participants with mild to moderate airflow limitation	• Adverse events • Vital Signs • Electrocardiogram (ECG) • Clinical Laboratory Assessments (haematology, clinical chemistry, urinalysis, and/or other safety biomarkers)
• To further characterize the clinical activity of danirixin HBr 35mg tablets compared with placebo	• Time to first HCRU COPD exacerbation • Change from baseline in FEV_1 (post-bronchodilator) • SGRQ responder analysis • SGRQ domains • COPD Assessment Test (CAT) • Rescue medication use

2.3. Study Design

Overview of Study Design and Key Features



[1] If changes to medication are required, consent must be signed prior to any changes being made and may occur prior to the Screening Visit

[2] Follow-up visit to occur within 28 days of last dose of study medication

Design Features	• This study will be conducted as a multi-centre, randomized, double-blind, sponsor open, placebo-controlled, 52-week study investigating the potential impact of danirixin HBr 35mg tablets compared with placebo on disease progression in participants with mild to moderate airflow obstruction. • Participants will be randomized 1:1 to either danirixin HBr 35mg or placebo. The randomization will be stratified based on smoking status (current or former smokers).
Dosing	• Study treatment will be administered twice daily for 52 weeks.
Time & Events	• Refer to Appendix 2: Schedule of Activities
Treatment Assignment	• Participants will be randomized (1:1) to receive either danirixin HBr 35mg or placebo. Participants will be instructed to take one tablet twice daily with food • GSK RandAll NG used to generate randomization schedules. • Randomization will be stratified based on smoking status (former vs. current)
Interim Analysis	• No interim analysis is planned for the study.

2.4. Statistical Analyses

Due to the early termination of the study, the primary efficacy endpoint cannot be met and no formal analysis will be done with the small number of participants contributing minimal data. The core safety summaries and available summary statistics for primary and secondary endpoints will be presented.

3. PLANNED ANALYSES

3.1. Final Analyses

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

1. All participants have completed the final (early withdrawal) visit, are deemed lost to follow-up or are deceased.
2. All required database cleaning activities have been completed and final database release (DBR) has been declared by Data Management.
3. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed according to RandAll NG procedures and study is unblinded.
5. Database freeze (DBF) is declared by Data Management.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Subjects	• All participants who were screened for eligibility and for whom a record exists on the study database and will be used for the tabulation, listing of reasons for withdrawal before randomization and listings of AEs and SAEs for nonrandomized participants.	• Subject Disposition • Reasons for withdrawal before randomization. • Inclusion, exclusion, and randomization criteria deviations
Safety	• This population will comprise all participants randomized to treatment, excluding those who were randomized in error (participants randomized in error will be recorded as screen failures), who take at least one dose of study treatment. Participants will be analysed according to the treatment they actually received. • This will constitute the primary population for all analyses and summaries of efficacy and safety. Outcomes will be reported according to the actual treatment allocation.	• Safety • Primary analysis • Study Population • Efficacy • Health-related Quality of Life Assessments • Inhaler Assessments

NOTES: Please refer to Appendix 10: List of Data Displays which details the population to be used for each display being generated.

4.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarised and listed. (Please refer to Appendix 1: Protocol Deviation Management).

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the most current Protocol Deviation Management Plan.

- Data will be reviewed prior to unblinding and freezing the database (DBF) 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 electronic case report form (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 HBr	2

Treatment comparisons will be displayed as follows using the descriptors as specified:
Danirixin vs. Placebo

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment with a non-missing value, 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.

Parameter	Study Assessments Considered as Baseline		Baseline Used in Data Display
	Screening	Week 0/ Day 1	
FEV_1 (All Spirometry)	X	X	Week 0/Day 1
SGRQ-C Total Score		X	Week 0/Day 1
SGRQ-C Domain Scores		X	Week 0/Day 1
CAT score		X	Week 0/Day 1
Vital Signs	X	X	Week 0/Day 1
ECG	X	X	Week 0/Day 1
Clinical Laboratory Assessments	X	X	Week 0/Day 1
Rescue Medication Use: Mean number of occasions per day	X	X	-7 to -1 (Mean during a stable period between 7 days before treatment start date (Week 0/Day 1) and day before Day 1 of study treatment. Data must be present on at least 4 days.)
Rescue Medication Use: Percentage of rescue-free days	X	X	-7 to -1 (Mean during a stable period between 7 days before treatment start date (Week 0/Day 1) and day before Day 1 of study treatment. Data must be present on at least 4 days.)

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

5.3. Spirometry and Rescue Medication Use Sources

5.3.1. Spirometry Sources

Clinic (centralized) spirometry collecting FEV_1 and FVC measurements (FEV%, and FVC% and FEV1/FVC will be calculated) will be performed in triplicate at time points listed in the SoA at the clinic. All spirometry values used and presented will be based on clinic spirometry.

Mobile (handheld) spirometry collecting FEV_1 and FVC parameters will also be performed weekly outside of clinic visits by the participants using a handheld spirometer at home.

5.3.2. Rescue Medication Use Sources

Rescue medication use will be collected via a daily diary over the course of the study.

Metered Dose Inhalers (MDI) sensor devices will be attached to participants' rescue medications and the date and time of each use of rescue medication will be recorded and transmitted.

Both rescue medication use from daily diary and MDI sources will be reported.

5.4. Other Considerations for Data Analyses and Data Handling Conventions

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

Section	Component
10.3	Appendix 3: Assessment Windows
10.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
10.5	Appendix 5: Data Display Standards & Handling Conventions
10.6	Appendix 6: Derived and Transformed Data
10.7	Appendix 7: Reporting Standards for Missing Data
10.8	Appendix 8: Values of Potential Clinical Importance

6. 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 participants' disposition, protocol deviations, medical history, 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 10: List of Data Displays.

7. EFFICACY ANALYSES

7.1. Primary Efficacy Analyses

7.1.1. Variables

7.1.1.1. FEV_1

Post-bronchodilator FEV_1 (L) (from clinic spirometry) to measure change in lung function will be summarized as specified in Section 7.1.2.

The table below shows the schedule of pre- and post-bronchodilator clinic spirometry assessments by visit.

Assessment	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	EW
Pre-bronchodilator													
FEV_1 (L)	X												
FVC (L)	X												
Post-bronchodilator													
FEV_1 (L)	X	X	X	X	X	X	X	X	X	X	X	X	X
FVC (L)	X	X	X	X	X	X	X	X	X	X	X	X	X

7.1.1.2. SGRQ Total Score

St. George Respiratory Questionnaire (SGRQ) total score derived from SGRQ-C at each scheduled visit will be summarized as specified in Section 10.5.2 and Section 10.6.3.

7.1.2. Summary Measure

Summary statistics, as specified in Section 10.5.2, for FEV_1 (L) and SGRQ total scores by treatment for each time point

7.1.3. Population of Interest

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

7.1.4. Strategy for Intercurrent (Post-Randomization) Events

Should any participant discontinue treatment (prior to project termination announcement), any recorded data up to the time of treatment discontinuation will be used in summaries.

Any intermittent missing data, not due to treatment discontinuation, will remain missing and any subsequent available data will be used.

7.1.5. Methods

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

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

7.2. Secondary Efficacy Analyses

7.2.1. Variables

7.2.1.1. Spirometry

Percent predicted FEV_1, FVC (L) and FEV_1/FVC (from clinic spirometry) will be summarized as specified in Section 7.2.2.

7.2.1.2. SGRQ Domain Scores

Raw and change from baseline SGRQ Domain scores will be summarized as specified in Section 7.2.2.

7.2.1.3. CAT

Raw and change from baseline CAT scores will be summarized as specified in Section 7.2.2.

7.2.1.4. Rescue Medication Use

The 4-week mean number of puffs/occasions of rescue use per day and percentage of rescue-free days according to daily eDiary data and MDI sensor data will be summarized as specified in Section 7.2.2.

7.2.2. Summary Measure

Summary statistics as specified in Section 10.5.2, for percent predicted FEV_1, FVC (L), FEV_1/FVC, SGRQ domain scores and CAT scores by treatment for each time point

Rescue medication use, from both daily diary and MDI sources, will be summarized as mean number of puffs/occasions of rescue use per day and percentage of rescue-free days in 4-week periods as specified in Section 10.6.3.

7.2.3. Population of Interest

The summary of secondary endpoints will be based on the Safety population, unless otherwise specified.

7.2.4. Methods

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

Unless otherwise specified, variables defined in Section 7.2.1 will be summarized using descriptive statistics.

8. SAFETY ANALYSES

All core safety outputs will be reported. 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.

8.2. Adverse Events of Special Interest Analyses

AESI have been defined as AEs which have specified areas of interest for the COPD population. A comprehensive list of Standardized Medical Dictionary for Regulatory Activities (MedDRA) terms based on clinical review will be used to identify each type of event. A list is provided in Section 10.6.4.

8.3. Clinical Laboratory Analyses

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

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 10: List of Data Displays.

9. REFERENCES

CAT Development Steering Group. COPD assessment test—healthcare professional user guide, Issue 3: December 2016.

Jones PW, Forde Y. (2016) St. Georges Respiratory Questionnaire for COPD Patients Manual, version 1.3

10. APPENDICES

10.1. Appendix 1: Protocol Deviation Management

10.1.1. Protocol Deviation Management

Protocol Deviations in accordance with the most recent Protocol Deviation Management Plan will be tracked by the study team throughout the conduct of the study and at the final protocol deviation review at DBR. Important protocol deviations will be identified and listed as defined in Appendix 10.

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10.2. Appendix 2: Schedule of Activities

10.2.1. Protocol Defined Schedule of Events

	Screening/ Visit1[a]	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8**	**Visit 9**	**Visit 10**	**Visit 11**	**Visit 12**	**EW**	**FU** Up to 28 days post last dose
	up to -32 days	Week 0 / D1	Week 2/ D14	Week 4/ D28	Week 8/ D56	Week 12/ D84	Week 16 / D112	Week 20 / D140	Week 24 /D168	Week 32 /D224	Week 40 / D280	Week 52 / D364		
Assessment window		+3d	±3d	±3d	±3d	±3d	±3d	±3d	±3d	±6d	±6d	±6d	±6d	
Eligibility														
Informed Consent	X													
Genetics Informed Consent[b]	X													
Demography	X													
Inclusion and Exclusion Criteria	X													
Smoking Status[c]	X	X												
Smoking History[c]	X													
Medical History[d]	X													
Full physical	X													
Chest X-ray (historical within 1 year acceptable)	X													
HIV, Hepatitis B and C screening[e]	X													
Additional Eligibility and In Study Assessments														
Verify Eligibility[f]	X	X												
Brief physical		X				X			X			X	X	
Laboratory assessments (clinical chemistry, including liver chemistries), haematology, urinalysis	X	X		X					X			X	X	
Additional Liver chemistries only			X		X	X	X	X		X	X			
12 lead ECG	X	X		X		X			X			X	X	
Vital Signs	X	X		X		X			X			X	X	

	Screening/ Visit1[a]	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8**	**Visit 9**	**Visit 10**	**Visit 11**	**Visit 12**	**EW**	**FU** Up to 28 days post last dose
	up to -32 days	Week 0 / D1	Week 2/ D14	Week 4/ D28	Week 8/ D56	Week 12/ D84	Week 16 / D112	Week 20 / D140	Week 24 /D168	Week 32 /D224	Week 40 / D280	Week 52 / D364		
Assessment window		+3d	±3d	±3d	±3d	±3d	±3d	±3d	±3d	±6d	±6d	±6d	±6d	
Office spirometry (centralized)	X	X	X	X	X	X	X	X	X	X	X	X	X	
Home spirometry - (weekly)	X	←	—	—	—	—	—	—	—	—	→	X	X	
Randomization		X												
Dispense study medication		X		X	X	X	X	X	X	X	X			
Dispense log pad and provide training	X													
Dispense MDI sensors and provide training	X													
Study Treatment		←	—	—	—	—	—	—	—	—	→			
Study Treatment Compliance (ediary)		←	—	—	—	—	—	—	—	—	→			
Collect IP				←	—	—	—	—	—	—	→			
Collect MDI sensors												X	X	
Collect log pad												X	X	
AE review		←	—	—	—	—	—	—	—	—	→		X	X
SAE review	←	—	—	—	—	—	—	—	—	—	→		X	X
Concomitant medication review	X	X	X	X	X	X	X	X	X	X	X	X	X	
Clinical Outcomes Assessments														
COPD exacerbation review		X	X	X	X	X	X	X	X	X	X	X	X	
Rescue medication Use	←	—	—	—	—	—	—	—	—	—	—	→		
SGRQ-C		X				X			X	X		X	X	
COPD Assessment Test (CAT)		X				X			X	X		X	X	
Participant Global Impression of COPD severity	X													
Participant Impression of change in COPD severity			X	X	X	X	X	X	X	X	X	X	X	

	Screening/ Visit1[a]	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8**	**Visit 9**	**Visit 10**	**Visit 11**	**Visit 12**	**EW**	**FU** Up to 28 days post last dose
	up to -32 days	Week 0 / D1	Week 2/ D14	Week 4/ D28	Week 8/ D56	Week 12/ D84	Week 16 / D112	Week 20 / D140	Week 24 /D168	Week 32 /D224	Week 40 / D280	Week 52 / D364		
Assessment window		+3d	±3d	±3d	±3d	±3d	±3d	±3d	±3d	±6d	±6d	±6d	±6d	
Genetic, Pharmacokinetic and Biomarker Blood Collections														
Blood sample for Genetics		X												
Blood sample for CRP		X							X			X	X	
Blood sample for exploratory biomarkers		X							X			X	X	

a Informed consent may be signed prior to screening visit in the case that any changes in medications are necessary

b Agreeing to genetic sample consent is not required for study participation

c Smoking status/history assessed at screening; smoking status re-checked at Visit 2

d Includes substance usage, past and present medical conditions and family history of premature CV disease

e 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 RNA testing is optional; however a confirmatory negative Hepatitis C RNA test must be obtained, to be able to enrol participants with positive Hepatitis C antibody due to prior resolved disease.

f Participant's clinical status should be reviewed

10.3. Appendix 3: Assessment Windows

10.3.1. Definitions of Assessment Windows for Analyses

In general, data will be reported according to the nominal time of clinic visits and assessments as specified in the protocol. For example, if a participant recorded values for the Day 28 visit that were actually made on the 21st day of treatment, they will be presented as Day 28 values in the summary tables.

Participants that withdraw from the study at the time of a scheduled study visit will have data collected in the eCRF as part of the scheduled study visit. In order to collect all questionnaires that are scheduled to be performed at the Early Withdrawal (EW) Visit, Patient Reported Outcomes questionnaires completed on the LogPad will be reported as an EW Visit. If the date of the EW questionnaire assessment is the same as the date of a scheduled visit date from the eCRF and there is no questionnaire assessment present at the scheduled visit in question, the EW questionnaire data will be listed, summarized and analysed as part of the scheduled visit.

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

10.4.1. Study Phases

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

Study Phase	Definition
Pre-Treatment	Date (and time) ≤ Study Treatment Start Date (and time)
On-Treatment	Study Treatment Start Date (and time) < Date (and time) ≤ Study Treatment Stop Date + 3 days
Post-Treatment	Date > Study Treatment Stop Date + 3 days

10.4.1.1. Study Phases for Concomitant Medication

COPD medication combinations taken at screening will include all COPD medications that were taken on the day of the screening visit, excluding medications that stopped on the day of the screening visit.

Treatment phases for summaries of COPD and non-COPD concomitant medications will be classified as follows:

Study Phase	Definition
Prior to Treatment	Medications taken on or before the day before treatment start date defined as: (conmed start date < treatment start date or 'Taken prior to study?' is 'Yes' or study treatment not started or conmed start date is missing) Note: Prior concomitant medication data will only be summarized for COPD medications. COPD concomitant medications that have been stopped greater than three calendar months prior to Visit 1 and non-COPD concomitant medications that have been stopped prior to randomization will not be included in any summary tables
On-treatment	If study treatment stop date > study treatment start date, then this includes medications taken between the study treatment start date and study treatment stop date - 1 (inclusive) defined as follows: (conmed start date < study treatment stop date or conmed start date is missing) and (conmed stop date >= study treatment start date or (conmed stop date is completely missing and study treatment start date is non-missing)) If study treatment stop date = study treatment start date, then this includes medications taken on the study treatment start date (which is equal to the study treatment stop date) defined as follows. (conmed start date <= study treatment stop date or conmed start date is missing) and (conmed stop date >= study treatment start date or (conmed stop date is completely missing and study treatment start date is non-missing))
Post-treatment	If study treatment stop date > study treatment start date, then this includes medications taken after the study treatment stop date defined as follows: (conmed stop date >= study treatment stop date or (conmed stop date is completely missing and study treatment stop date is non-missing)) If study treatment stop date = study treatment start date, then this includes medications

Study Phase	Definition
	taken after the study treatment stop date + 1 defined as follows. (conmed stop date > study treatment stop date or (conmed stop date is completely missing and study treatment stop date is non-missing))

NOTES:

- A concomitant medication will be classed in every period of the study in which it was taken.
- See Section 10.7.2.1 for handling of partial dates.
- If the study treatment stop date is missing, it will be imputed as described in Section 10.6.1.

10.4.1.2. Study Phases for Event Data

Classification of an AE as having onset on-treatment will be made with reference to the study treatment start and stop dates and the event onset date. If the event onset date is missing, then the event will be considered on-treatment.

Study Phase	Definition
Pre-treatment	If onset date is prior to treatment start date Start Date < Study Treatment Start Date
On-treatment	If onset date is on or after treatment start date & on or before treatment stop date + 3 days. Study Treatment Start Date ≤ Start Date ≤ Study Treatment Stop Date + 3 days
Post-treatment	If onset date is after treatment stop date + 3 days. Start Date > Study Treatment Stop Date + 3 days

Note: assume on-treatment unless there is evidence to the contrary

10.4.1.3. Treatment Emergent AEs

If the study treatment stop date is missing, it will be imputed as described in Section 10.6.1.

Flag	Definition
Treatment Emergent	If AE onset date is on or after treatment start date & on or before the treatment stop date + 3 days • Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date + 3 days

NOTES:

- Time of study treatment dosing and start/stop time of AEs should be considered, if collected.

10.5. Appendix 5: Data Display Standards & Handling Conventions

10.5.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: uk1salx00175
HARP Compound	: GSK1325756
Analysis Datasets	
• Analysis datasets will be created according to IDSL standards.	
Generation of RTF Files	
• RTF files will be generated for the final reporting effort	

10.5.2. Reporting Standards

General

- The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated (IDSL Standards Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  - 4.03 to 4.24: 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 (4.24) 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 the 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.
  - SGRQ will have a min and max to 1 decimal places (dp) and then follow IDSL standards for reporting other summary statistics.
  - CAT will have a min and max to 0 dp and then follow IDSL standards for reporting other summary statistics.
- Categories will be based on rounded values to the precision collected on the eCRF or vendor provided data
- Summary Statistics of continuous data will include number or participants, mean, SD, median, minimum and maximum.

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 except as part of a maximum/minimum/worst case post-baseline assessment • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

10.6. Appendix 6: Derived and Transformed Data

10.6.1. General

Multiple Measurements at One Analysis Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • If there are two values within a time window (as per Section 10.3.1) 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. • 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 Date ≥ First Dose Date → Study Day = Ref Date – (First Dose Date) + 1

Study Treatment Stop Date
• If the study treatment stop date is missing, it will be imputed as follows: • If any of EW Visit date, Visit 12 (Week 52/Day 364) date or date of death are non-missing then the study treatment stop date will be imputed as the minimum of (EW Visit date, Visit 12 (Week 52/Day 364) date, date of death, date that all study treatment containers were returned). For all other missing treatment stop dates, the last recorded exposure start or stop date will be used.
Study Completion Definition
• A participant is considered to have completed the study if they have not withdrawn and attended Visit 12.

10.6.2. Study Population

Demographics
Age

• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
  ○ 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'.
• Age will be calculated based on the screening visit date.
• Age group categories are 18-64, 65-74, 75-84

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

Baseline Characteristics

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

COPD Exacerbation (Historical) Categories

- Moderate/severe historical exacerbations are defined as those requiring oral/systemic corticosteroids and/or antibiotics or hospitalisation.
- The number of exacerbations requiring oral/systemic corticosteroids and/or antibiotics, the number requiring hospitalisation and the number of moderate/severe COPD exacerbations for each participant will be categorized as 0, 1, ≥2 for summary displays.

GOLD Grade 1-4 at Screening

- Participants will be classified into Global Initiative on Obstructive Lung Disease (GOLD) Grades 1-4 using the post-bronchodilator percent predicted FEV_1 assessment at Screening:
  - GOLD Grade 1 (Mild): percent predicted FEV_1 ≥80%
  - GOLD Grade 2 (Moderate): 50%≤ percent predicted FEV_1 <80%
  - GOLD Grade 3 (Severe): 30%≤ percent predicted FEV_1 <50%
  - GOLD Grade 4 (Very Severe): percent predicted FEV_1 <30%

GOLD Grade A-D at Screening

- Participants will be classified into GOLD Grades A-D definitions as follows:

  A. Low risk, less symptoms: baseline CAT < 10 AND GOLD Grade 1-2 AND ≤1 exacerbation; (no hospitalizations for exacerbations), prior year.

  B. Low risk, more symptoms: baseline CAT >= 10 AND GOLD Grade 1-2 AND ≤1 exacerbation (no hospitalizations for exacerbations), prior year

  C. High risk, less symptoms: baseline CAT < 10 AND either GOLD Grade 3-4 OR ≥ 2 exacerbations, prior year OR >=1 exacerbation leading to hospitalization, prior year

  D. High risk, more symptoms: baseline CAT >= 10 AND either GOLD Grade 3-4 OR ≥ 2 exacerbations, prior year OR >=1 exacerbation leading to hospitalization, prior year

Concomitant Medications

Respiratory Medication Class

- COPD concomitant medications will be grouped into the following RMCs based on pre-defined code lists derived from ATC classifications:
  - Androgens and Estrogens
  - Anti-IgE, Anti-IL5
  - Anticholinergic
  - Antiinfectives (antibiotics, antiseptics only)
  - Antimycotics
  - Antivirals
  - Beta 2 Agonist
  - Corticosteroid – Inhaled
  - Corticosteroid – Depot
  - Corticosteroid – Systemic, oral, parenteral and intra-articular
  - Corticosteroid – Other
  - Leukotriene Receptor Antagonist
  - Long-acting anticholinergic

○ Long-acting beta-2 agonist ○ Mucolytics ○ Nedocromil or Cromolyn Sodium ○ Oxygen ○ PDE4 Inhibitors ○ Short-acting anticholinergic ○ Short-acting beta-2 agonist ○ Xanthine ○ Other medication given for exacerbation ○ Other COPD medication
COPD Medication Combination
• COPD medications will be summarized at the following time points: ○ At Screening: Taken on the day of the Screening visit excluding medications that stopped on the day of the Screening visit • Medication combinations of all RMC categories will be derived. Medications will be summarized based on individual and combinations of the following RMC categories, with or without other medications: ○ ICS ○ LABA ○ LAMA ○ Xanthine ○ PDE4 inhibitor ○ Anti-IgE, Anti-IL5

Exposure
Exposure to Study Treatment
Duration of exposure to study treatment is calculated as (treatment stop date – treatment start date +1). The following exposure categories will be derived: ≥1 day, ≥2 weeks, ≥4 weeks, ≥8 weeks, ≥12 weeks, ≥16 weeks, ≥20 weeks, ≥ 24 weeks, ≥32 weeks, ≥40 weeks and ≥52 weeks.

10.6.3. Efficacy

SGRQ
SGRQ-C Total and Domain Scores
• The SGRQ-C contains 40 questions grouped into three domains (Symptoms, Activity and Impacts). • Details for how to score the SGRQ-C, including handling of missing data or multiple responses to questions, are outlined in the SGRQ-C manual (Jones, 2016). • SGRQ-C total and domains scores will be converted to SGRQ scores as described in the manual. • Changes from baseline in total and domain scores will be calculated for the converted scores. • If the language of the SGRQ-C conducted at a post-baseline visit is different to the language used at baseline, all SGRQ scores at that visit and all subsequent visits will be set to missing.

CAT
CAT Score
• The CAT consists of eight items each formatted as a six-point differential scale: 0 (no impact) to 5 (high

impact). A CAT score will be calculated by summing the non-missing scores on the eight items. The score can have values ranging from 0 to 40.

- If one item is missing, then the score for that item is set as the average of the non-missing items. If more than one item is missing, then the CAT score will be set to missing.
- If the language of the CAT conducted at a post-baseline visit is different to the language used at baseline, the CAT score for that visit and all subsequent visits will be set to missing.
- If there is more than one response to a question at a visit or duplicate questionnaires, the CAT score for that visit will be set to missing.

Rescue Medication Use

Daily eDiary

- Participants were instructed to complete the daily eDiary in the evening (typically at bedtime) to collect the number of puffs of rescue mediation(s) over each 24-hour period.
- The table below shows which daily rescue medication use records are to be used to calculate summaries for each period. Any daily rescue medication use data collected after the minimum of (Day 364 or the day before study treatment stop date) will not be slotted.

Period	First day	Last day
Baseline [1]	Day -7	Day -1
Weeks 1 – 4[1]	Day 1	Day 28
Weeks 5 – 8[1]	Day 29	Day 56
Weeks 9 – 12[1]	Day 57	Day 84
Weeks 13 – 16[1]	Day 85	Day 112
Weeks 17 – 20[1]	Day 113	Day 140
Weeks 21 – 24[1]	Day 141	Day 168
Weeks 25 – 28[1]	Day 169	Day 196
Weeks 29 – 32[1]	Day 197	Day 224
Weeks 33 – 36[1]	Day 225	Day 252
Weeks 37 – 40[1]	Day 253	Day 280
Weeks 41 – 44[1]	Day 281	Day 308
Weeks 45 – 48[1]	Day 309	Day 336
Weeks 49 – 52[1]	Day 337	Earliest of (Study day 364 and day before study treatment stop date)

[1] The denominator for baseline and 4-week mean scores is the number of days with a non-missing score; this is also used to determine whether a baseline (>=4 days) or 4-week mean (>=10 days) is calculated or not.

- If a participant has more than one daily diary record for any given day, the worst-case response on that day for each endpoint will be used in the summaries and analyses. i.e. the maximum number of puffs of rescue use reported will be counted for the day in question and used to determine if it was a recue-free day.
- A rescue-free day is defined as a day where the total puffs is 0.
- For each summary period, the mean number of puffs per day and the percentage of rescue free days, will be calculated, using the number of days with non-missing values for the endpoint as denominator.
- Rescue use will be summarized over the periods defined above.

Metered Dose Inhaler (MDI) Sensor

- The MDI Sensor will be attached to the participant's rescue medication(s). The MDI Sensor will transmit its medication use data to the LogPad provided by ERT via a Bluetooth connection.

• The mean number of occasions of rescue per day and the percentage of rescue-free days will be calculated over the same time periods and using the same assumptions as rescue use via diary. • Rescue-free Days - days within the diary data collection period with no recorded rescue inhaler usage by the sensor will be assigned a rescue inhaler usage of 0.

10.6.4. Safety

Adverse Events
AEs of Special Interest
• AESI are defined as events in the 'Infective pneumonia' SMQ in the MedDRA version current at the time of reporting.

Maximum/Minimum Post-Baseline and Worst-Case Post-Baseline	
Definition	**Reporting Details**
Maximum post-baseline (QTcF, QTcB, PR interval, ECG heart rate, pulse rate, systolic BP, diastolic BP and laboratory tests)	Change from baseline of maximum value over all time-points after Day 1
Minimum post-baseline (Diastolic BP and laboratory tests that do not have a lower limit = 0)	Change from baseline of minimum value over all time-points after Day 1
Worst case post-baseline (ECG findings)	• 'Abnormal' if any on-treatment assessment is evaluated as 'Abnormal' • 'Unable to evaluate' if all on-treatment assessments are 'Unable to evaluate' • 'Normal' if any on-treatment assessment is evaluated as 'Normal' and there are no on-treatment assessments evaluated as 'Abnormal'

NOTES:

- The treatment phase definitions specified in Section 10.4.1 will be used and only assessments within the on-treatment period will be considered in assessment of minimum/maximum/worst-case post-baseline.
- Assessment of minimum/maximum/worst-case post-baseline will include on-treatment data from scheduled, unscheduled and study treatment discontinuation visits (if applicable)

Laboratory Parameters
General
• NQ laboratory results will be treated as missing in summary displays. However, the results will be listed as received (e.g. '<x' or '>x'). • A 'worst case post-baseline' change classification will be derived, in which participants will be counted in the 'to low' and 'to high' categories if they reported a change from an 'in range' baseline to a value below or above the PCI criteria (respectively) at any scheduled or unscheduled on-treatment visit. Participants who did not report a change to a value outside the PCI criteria at any visit after the start of study treatment will be counted in the 'to w/in range or no change' category.
Multiple Measurements for On-Treatment Visits for Safety

Laboratory Parameters
General
• Participants having both high and low values relative to PCI criteria at post-baseline visits for safety parameters will be counted in both the high and low categories of the "worst case post-baseline" row of related summary tables.

ECG
General
• The QTc data was collected via machine derived values (QTCB/QTCF) or manually derived values (QTCBC/QTCFC). For the purposes of reporting the following variable should be combined: - Combine QTCF with QTCFC • If both QTCF and QTCFC are missing (and QT and RR are non-missing, then the QTcF interval will be derived as follows: - QTcF interval (msec) = QT/[(RR/1000)**(1/3)] - If RR interval is not collected and the corrected QT interval by Bazett's method (QTcB) is collected, then RR interval (msec) will be derived prior to deriving QTcF as follows: RR interval (msec) = 1000*[(QT/QTcB)**2] • If QTcF intervals are collected they will not be rederived.
ECG Categories
Maximum and maximum increase in QTcF values will be reported in categories as below. In participants who have QTc above 450 at baseline, decreases that result in a QTc that remains above 450 will be considered No Change.

ECG Parameter	Units	Category
Absolute		
Absolute QTcF Interval	msec	No Change or Decrease to <=450
		Increase To >450 to <=480
		Increase To >480 to <=500
		Increase To >500
Change from Baseline		
Change from Baseline QTcF	msec	Increase of <=30 msec
		Increase of 31-60 msec
		Increase of >60 msec

Assessment of maximum post-baseline will include on-treatment data from scheduled, unscheduled and study treatment discontinuation visits (if applicable)

10.7. Appendix 7: Reporting Standards for Missing Data

10.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion (i.e. as specified in the protocol) was defined as completion of all phases of the study including the last study visit and the last scheduled procedure shown in the Schedule of Activities (Appendix 2) • For the purposes of reporting, a participant is considered to have completed the study if they have not withdrawn and attended Visit 12 • Withdrawn participants were not replaced in the study. • All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified. • Withdrawal visits will be slotted as per Appendix 3: Assessment Windows or will be summarised as withdrawal visits.

10.7.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: ○ 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	• If outliers are identified, analyses may be repeated excluding the outlying data • Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

10.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in 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.
Concomitant Medications/	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention:

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

10.8. Appendix 8: Values of Potential Clinical Importance

10.8.1. Laboratory Values

The following table identifies a range of potential clinical importance (PCI) for each laboratory analyte. Limits with an 'x' are multipliers of the central laboratory normal range. Values above and below this range will be considered of PCI.

Haematology 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
Reticulocyte Count (%)			>4%
Haemoglobin (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
MCHC (g/dL)		0.85x	1.10x
Neutrophils (%)		0.65x	1.50x
Lymphocytes (%)		0.80x	1.20x
Monocytes (%)		0.80x	1.60x
Eosinophils (%)			2.00x
Basophils (%)			5.00x

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 fasting (mmol/L)		<0.6x	>4x
Sodium (mmol/L)		0.80x	1.15x
Potassium (mmol/L)		0.75x	1.30x
Chloride (mmol/L)		0.90x	1.10x
Bicarbonate (mmol/L)		<18 mmol/L	>32 mmol/L
Calcium (mmol/L)		0.85x	1.08x
GGT (U/L)		0.85x	1.10x
Uric Acid (mg/dL)	Males	<2.1 mg/dL	>8.5 mg/dL
	Females	<2.0 mg/dL	>7.0 mg/dL
Albumin (mmol/L)		0.90x	1.50x
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
Total Bilirubin	High	≥ 2x ULN	μmol/L
Direct Bilirubin	High	≥ 2x ULN	μmol/L
Total Bilirubin + ALT	High	≥ 2x ULN Total Bilirubin + ≥ 3x ULN ALT	μmol/L U/L

10.8.2. ECG

ECG Parameter	PCI Range	Unit
Absolute QTc Interval (QTcB, QTcF)	>530	msec
Increase from Baseline QTcB,QTcF	>60	msec
QT Interval	<300 or >500	msec
PR Interval	<120 or >240	msec
QRS Interval	<70 or >125	msec
RR Interval	<375 or >1714	msec
Heart Rate	<35 or >120	bpm

10.8.3. Vital Signs

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

10.9. Appendix 9: Abbreviations & Trade Marks

10.9.1. Abbreviations

Abbreviation	Description
AE	Adverse Event
AESI	Adverse Event of Special Interest
ATC	Anatomical Therapeutic Chemical Classification
BD	Bronchodilator
BP	Blood Pressure
BUN	Blood urea nitrogen
CAT	COPD Assessment Test
COPD	Chronic Obstructive Pulmonary Disease
CSR	Clinical Study Report
DBF	Database Freeze
DBR	Database Release
DP	Decimal Places
ECG	Electrocardiogram
eCRF	Electronic Case Record Form
EW	Early Withdrawal
EudraCT	European Clinical Trials Database
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
FEV_1	Forced Expiratory Volume in 1 Second
FVC	Forced Vital Capacity
GGT	Gamma-glutamyl transferase
GOLD	Global Initiative for Obstructive Lung Disease
GSK	GlaxoSmithKline
HCRU	Healthcare Resource Utilization
IDSL	Integrated Data Standards Library
ICH	International Conference on Harmonization
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Microtic cell volume
MDI	Metered Dose Inhaler
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed Model Repeated Measures
NQ	Non-quantifiable
PCI	Potential Clinical Importance
PD	Protocol Deviations
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RMC	Respiratory Medication Class
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event

Abbreviation	Description
SD	Standard Deviation
SGOT	Serum glutamic oxalocaetic transaminase
SGPT	Siamane glutamate pyruvate transaminase
SGRQ	St. George's Respiratory Questionnaire
SGRQ-C	SGRQ for COPD patients
SMQ	Standardized MedDRA Query
ULN	Upper limit of normal

10.9.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
None

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS
ERT

10.10. Appendix 10: List of Data Displays

10.10.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.24	
Efficacy	2.1 to 2.15	
Safety	3.1 to 3.21	3.1 to 3.3
Section	**Listings**	
ICH Listings	1 to 37	

10.10.2. Deliverables

In all displays the term "Subjects" is used to refer to “Participants”.

Delivery	Description
SAC	Final Statistical Analysis Complete

10.10.3. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Safety	ES1	Summary of Subject Disposition for the Subject Conclusion Record	ICH E3, FDAAA, EudraCT	SAC
1.2.	All subjects	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements Specify Reasons for *Screening* Failure and include Reasons for Run-in Failure Section	SAC
1.3.	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment	ICH E3 Required for all studies except single dose studies	SAC
1.4.	Safety		Summary of Attendance at Each Clinic Visit	Including Screening	SAC
Protocol Deviation					
1.5.	Safety	DV1	Summary of Important Protocol Deviations	ICH E3	SAC
1.6.	All subjects	IE2	Summary of Inclusion/ Exclusion/ Randomization Criteria Deviations for Screen or Run-in failures	Add a row “Number of Screen Failures” above “any criteria deviations”. Percentage will be based on number of screen failures	SAC
1.7.	Safety	IE1	Summary of Inclusion/ Exclusion/ Randomization Criteria Deviations for the Safety Population		SAC
Population Analysed					

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.8.	All Subjects	SP1	Summary of Study Populations	IDSL	SAC
Demographic and Baseline Characteristics					
1.9.	Safety	DM1	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	SAC
1.10.	Safety	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT	SAC
1.11.	Safety	SU1	Summary of Smoking History and Smoking Status	Include smoking status, smoking pack years, cigarettes smoked/day	SAC
1.12.	Safety	SP_T12	Summary of COPD History at Screening		SAC
1.13.	Safety	SP_T1	Summary of HCRU Exacerbation History at Screening	See notes in Section 10.6.2 Include subgroups of Mild, Moderate, Severe, and Moderate/Severe	SAC
1.14.	Safety		Summary of GOLD Stages at Screening	GOLD 1-4 and GOLD A-D	SAC
1.15.	Safety		Summary of Screening Spirometry Measures	Pre-BD FEV_1 (L), Post-BD FEV_1 (L), Predicted normal FEV1 (L), Percent predicted normal post-BD FEV_1 (%), Post-BD FVC (L), Post-BD FEV_1/FVC	SAC
Past and Current Medical History					
1.16.	Safety	MH4	Summary of Past Medical Conditions	ICH E3	SAC
1.17.	Safety	MH4	Summary of Current Medical Conditions		SAC
Prior and Concomitant Medications					

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.18.	Safety	CM1	Summary of Non-COPD Concomitant Medications	ICH E3	SAC
1.19.	Safety	CM8	Summary of COPD Concomitant Medications Taken Pre-treatment		SAC
1.20.	Safety	CM8	Summary of COPD Concomitant Medications Taken On-Treatment, Medications Given for Reasons Other than an Exacerbation		SAC
1.21.	Safety	CM8	Summary of COPD Concomitant Medications Taken Post-treatment		SAC
1.22.	Safety	CM8	Summary of On-treatment COPD Concomitant Medications Given for an Exacerbation		SAC
1.23.	Safety		Summary of COPD Concomitant Medication Categories Taken at Screening	Number and percentage of participants taking each medication in the RMC categories defined in section 10.6.2	SAC
Exposure					
1.24.	Safety	EX1	Summary of Exposure to Study Treatment	ICH E3	SAC

10.10.4. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Spirometry					
2.1.	Safety	Based on PD4	Summary of Baseline Spirometry Measures	Post-BD FEV_1 (L), Percent predicted normal post-BD FEV_1 (%), Post-BD FVC (L), Post-BD FEV_1/FVC Transpose PD4 table to have treatment in columns and spirometry assessments in rows	SAC
2.2.	Safety	PD4	Summary of Post-Bronchodilator FEV1 (L)	Include raw and change from baseline	SAC
2.3.	Safety	PD4	Summary of Post-Bronchodilator FVC (L)	Include raw and change from baseline	SAC
SGRQ					
2.4.	Safety	PD4	Summary of Baseline SGRQ Scores	Total and domain scores	SAC
2.5.	Safety	PD4	Summary of SGRQ Scores by Visit	Include raw and change from baseline Total and domain scores	SAC
CAT					
2.6.	Safety	PD4	Summary of Baseline CAT Scores	Include total column	SAC
2.7.	Safety	PD4	Summary of CAT Score by Visit	Include raw and change from baseline	SAC
Rescue Medication Use					
2.8.	Safety	PD4	Summary of Baseline Mean Number of Puffs of Rescue Medication per Day using Diary Data	Include total column	SAC
2.9.	Safety	PD4	Summary of Baseline Percentage Rescue-free Days using Diary	Include total column	SAC

			Data		
2.10.	Safety	PD4	Summary of Mean Number of Puffs of Rescue Medication per Day using Diary Data in 4-week intervals		SAC
2.11.	Safety	PD4	Summary of Percentage Rescue-free Days using Diary Data in 4-week intervals		SAC
2.12.	Safety	PD4	Summary of Baseline Mean Number of Occasions of Rescue Use per Day using MDI Sensor Data	Include total column	SAC
2.13.	Safety	PD4	Summary of Baseline Percentage Rescue-free Days using MDI Sensor Data	Include total column	SAC
2.14.	Safety	PD4	Summary of Mean Number of Occasions of Rescue Use per Day using MDI Sensor Data in 4-week intervals		SAC
2.15.	Safety	PD4	Summary of Percentage Rescue-free Days using MDI Sensor Data in 4-week intervals		SAC

10.10.5. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	Safety	AE3	Summary of All Adverse Events by Preferred Term	ICH E3	SAC
3.2.	Safety	AE3	Summary of Common (>=5%) Adverse Events by Overall Frequency	ICH E3	SAC
3.3.	Safety	AE3	Summary All Drug-Related Adverse Events by Preferred Term	ICH E3	SAC
3.4.	Safety	AE15	Summary of Common (>=5%) Non-serious Adverse Events by Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT	SAC
Serious and Other Significant Adverse Events					
3.5.	Safety	AE16	Summary/Listing of Serious Adverse Events by Preferred Term [Number of Subjects and Occurrences]	FDAAA, EudraCT	SAC
3.6.	Safety	AE3	Summary of Pre-treatment Serious Adverse Events by Preferred Term		SAC
3.7.	Safety	AE3	Summary of On-treatment Serious Adverse Events by Preferred Term		SAC
3.8.	Safety	AE3	Summary/Listing of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by Preferred Term	IDSL	SAC
3.9.	Safety		Summary/Listing of On-treatment Adverse Events of Special Interest		SAC
Laboratory: Chemistry					

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.10.	Safety	LB1	Summary of Chemistry Changes from Baseline	ICH E3	SAC
3.11.	Safety	LB17	Summary/Listing of Worst Case Chemistry Results by Potential Clinical Importance Criteria (Post-Baseline Relative to Baseline)	ICH E3	SAC
Laboratory: Haematology					
3.12.	Safety	LB1	Summary of Haematology Changes from Baseline	ICH E3	SAC
3.13.	Safety	LB17	Summary/Listing of Worst Case Haematology Results by Potential Clinical Importance Criteria (Post-Baseline Relative to Baseline)	ICH E3	SAC
Laboratory: Hepatobiliary (Liver)					
3.14.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting	IDSL	SAC
3.15.	Safety	LIVER10	Summary/Listing of Hepatobiliary Laboratory Abnormalities	IDSL	SAC
ECG					
3.16.	Safety	EG1	Summary of ECG Findings	IDSL	SAC
3.17.	Safety	EG10	Summary/Listing of Maximum QTc Values Post-Baseline Relative to Baseline by Category	IDSL	SAC
3.18.	Safety	EG2	Summary of Change from Baseline in ECG Values by Visit	IDSL	SAC
3.19.	Safety	EG11	Summary/Listing of Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category	IDSL	SAC
Vital Signs					

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.20.	Safety	VS1	Summary of Change from Baseline in Vital Signs	ICH E3	SAC
3.21.	Safety	VS7	Summary of Worst Case Vital Signs Results by Potential Clinical Importance Criteria (Post-Baseline Relative to Baseline)	IDSL	SAC

10.10.6. Safety Figures

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
3.1.	Safety	AE10	Plot of Common (>=5%) Adverse Events and Relative Risk	IDSL	SAC
Laboratory					
3.2.	Safety	LIVER14	Scatter Plot of Maximum vs. Baseline for ALT	IDSL	SAC
3.3.	Safety	LIVER9	Scatter Plot of Maximum ALT vs. Maximum Total Bilirubin	IDSL	SAC

10.10.7. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	All Subjects	ES7	Listing of Reasons for Screen Failure	Journal Guidelines	SAC
2.	Safety	ES2	Listing of Reasons for Study Withdrawal	ICH E3	SAC
3.	Safety	SD2	Listing of Reasons for Study Treatment Discontinuation	ICH E3	SAC
4.	Safety	BL1	Listing of Subjects for Whom the Treatment Blind was Broken	ICH E3	SAC
5.	Safety	TA1	Listing of Planned and Actual Treatments	IDSL	SAC
Protocol Deviations					
6.	Safety	DV2	Listing of Important Protocol Deviations	ICH E3	SAC
7.	All Subjects	IE3	Listing of Screen Failure Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	SAC
8.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	SAC
Populations Analysed					
9.	All Subjects	SP3	Listing of Subjects Excluded from Any Population	ICH E3, safety	SAC
Demographic and Baseline Characteristics					
10.	Safety	DM2	Listing of Demographic Characteristics	ICH E3	SAC
11.	Safety	DM9	Listing of Race	ICH E3	SAC
Prior and Concomitant Medications					

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
12.	Safety	CP_CM3	Listing of COPD Concomitant Medications	IDSL	SAC
13.	Safety	CP_CM3	Listing of Non-COPD Concomitant Medications	IDSL	SAC
Exposure and Treatment Compliance					
14.	Safety	EX3	Listing of Exposure Data	ICH E3	SAC
Adverse Events					
15.	Safety	AE8	Listing of All Adverse Events	ICH E3	SAC
16.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	SAC
17.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	SAC
Serious and Other Significant Adverse Events					
18.	Safety	AE8	Listing of Fatal Serious Adverse Events	ICH E3	SAC
19.	Safety	AE8	Listing of Non-Fatal Serious Adverse Events	ICH E3	SAC
20.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	SAC
21.	Safety	AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	SAC
22.	Safety	AE8	Listing of Other Significant Adverse Events	ICH E3	SAC
23.	Safety	GCSP1	Listing of Treatment Details for Relevant Subjects	IDSL To be produced as a comma-delimited ASCII text file	SAC
Hepatobiliary (Liver)					

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
24.	Safety	MH2	Listing of Medical Conditions for Subjects with Liver Stopping Events	IDSL	SAC
25.	Safety	SU2	Listing of Substance Use for Subjects with Liver Stopping Events	IDSL	SAC
All Laboratory					
26.	Safety	LB5	Listing of Chemistry Data for Subjects with Any Value of Potential Clinical Importance	ICH E3	SAC
27.	Safety	LB5	Listing of Haematology Data for Subjects with Any Value of Potential Clinical Importance	ICH E3	SAC
28.	Safety	LB5	Listing of Chemistry Values of Potential Clinical Importance		SAC
29.	Safety	LB5	Listing of Haematology Values of Potential Clinical Importance		SAC
30.	Safety	LB14	Listing of Chemistry Data with Character Results		SAC
31.	Safety	LB14	Listing of Haematology Data with Character Results		SAC
ECG					
32.	Safety	EG3	Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance	IDSL	SAC
33.	Safety	EG3	Listing of ECG Values of Potential Clinical Importance	IDSL	SAC
34.	Safety	EG5	Listing of All ECG Findings for Subjects with an Abnormal ECG Finding	IDSL	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
35.	Safety	EG5	Listing of Abnormal ECG Findings	IDSL	SAC
Vital Signs					
36.	Safety	VS4	Listing of All Vital Signs Data for Subjects with Any Value of Potential Clinical Importance	IDSL	SAC
37.	Safety	VS4	Listing of Vital Signs of Potential Clinical Importance	IDSL	SAC