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

Title	:	Reporting and Analysis Plan for A Phase III, 52-week, Open-label Study to Evaluate Long-term Safety of Fixed Dose Combination Therapy Fluticasone Furoate/Umeclidinium Bromide/Vilanterol Trifenatate in Japanese Patients with Asthma
Compound Number	:	GSK573719+GW642444+GW685698
Effective Date	:	17-DEC-2018

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol [GSK Document Number 2016N305271_02].
- This RAP also describes the outputs to be produced for the interim analysis at 24 weeks.
- This RAP is intended to describe the safety and other 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):

Author	Date
PPD Statistician, Biostatistics Group 2, Biomedical Data Sciences, Japan	NA

RAP Team Review Confirmations:

Reviewer	Date
PPD Lead Programmer, Statistical Programming & Reporting Group, Biomedical Data Sciences, Japan	10-DEC-2018
PPD Japan Project Leader, Respiratory TA Office, Medicines Development, Japan	04-DEC-2018
PPD Clinical Investigation Lead, Respiratory TA Office, Medicines Development, Japan	10-DEC-2018
PPD Operations and Science Leader, Clinical Operation, Japan	07-DEC-2018
PPD Data Quality Lead, Data Practice Group, Biomedical Data Sciences, Japan	07-DEC-2018
PPD Medical Writer, Medical Writing Office, Medicines Development, Japan	06-DEC-2018

Clinical Statistics and Clinical Programming Line Approvals:

Approver	Date
PPD Manager (statistics), Biostatistics Group 2, Biomedical Data Sciences, Japan	13-DEC-2018
PPD Manager (programming), Statistical Programming & Reporting Group, Biomedical Data Sciences, Japan	17-DEC-2018

TABLE OF CONTENTS

PAGE

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 as well as the analyses to be included in the interim report for the protocol:

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the protocol (Dated: 13/MAR/2017), amendment 1 (Dated:24/MAY/2017) or amendment 2 (Dated: 25/OCT/2017).

In order to comply with regulatory guidance where the protocol referred to "Subjects" the analysis plan refers to "Participants", with the exception of displays and study populations.

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

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To evaluate the safety of long-term treatment with FF/UMEC/VI combination therapy	• Incidence and type of adverse events (AE)/serious adverse events (SAE)
Secondary Objectives	**Secondary Endpoints**
• To evaluate the safety of FF/UMEC/VI combination therapy	• Blood pressure/pulse measurements • 12-lead ECG • Clinical laboratory tests (hematology, biochemistry and urinalysis)
Other Objectives	**Other Endpoints**
• To evaluate the efficacy of FF/UMEC/VI combination therapy	• Mean change from baseline in trough Forced Expiratory Volume in 1 second (FEV_1) at Week 24 and Week 52[*1] • Mean change from baseline in ACQ-7 total score at Week 24 and Week 52[*1] • Mean change from baseline in St. George's Respiratory Questionnaire (SGRQ) total score at Week 24 and Week 52[*1] • Mean change from baseline in the Asthma Quality of Life Questionnaire (AQLQ) total score at Week 24 and Week 52[*1] • Unscheduled asthma-related healthcare resource utilization over the 52 weeks of the treatment

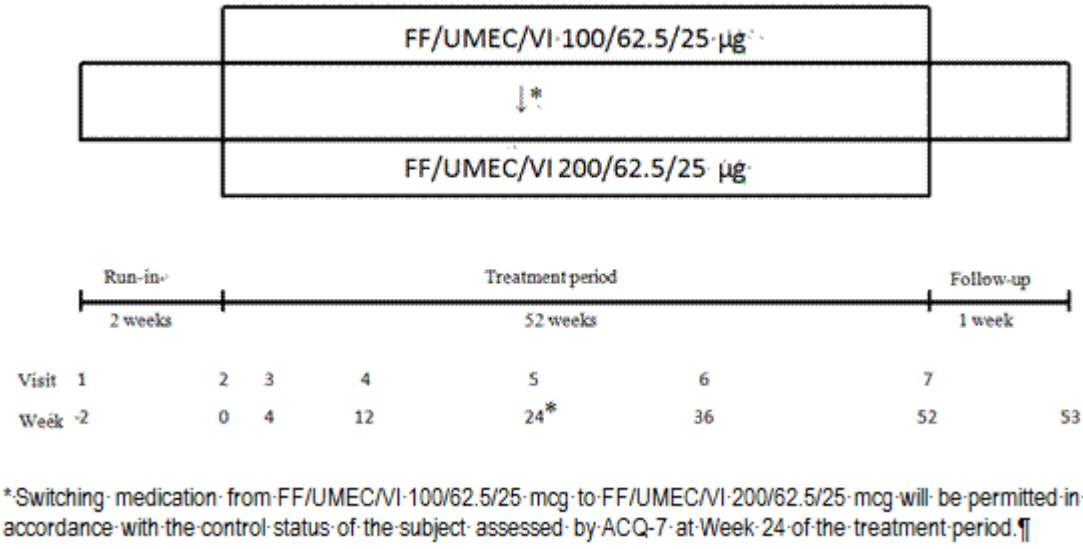
Objectives	Endpoints
	period*2 • Annualized rate of severe asthma exacerbations*2 • Annualized rate of moderate/severe asthma exacerbations*2

NOTES:

- *1: Week 24 will be presented for the interim and the final analysis. Week 52 will be presented for the final analysis only.
- *2: This will be presented for the final analysis only.

2.3. Study Design

Overview of Study Design and Key Features



*Switching medication from FF/UMEC/VI 100/62.5/25 mcg to FF/UMEC/VI 200/62.5/25 mcg will be permitted in accordance with the control status of the subject assessed by ACQ-7 at Week 24 of the treatment period.¶

Design Features	• The present study is a phase III, multicenter, non-comparator, non-randomized, open-label study in Japanese patients with asthma. This is an approximately 55-week study consisting of the run-in, treatment and follow-up periods. • The number of asthmatic adult subjects (with the control status on ICS [medium to high dose]/ LABA and/or LAMA) required to be enrolled in this study is 110 (a total number of participants to be allocated in Group 1 [FF/UMEC/VI 100/62.5/25] and Group 2 [FF/UMEC/VI 200/62.5/25]). There is NOT any target allocation ratio in Group 1 and Group 2. • Switching medication from FF/UMEC/VI 100/62.5/25 mcg to FF/UMEC/VI 200/62.5/25 mcg will be permitted in accordance with the control status of the subject assessed by ACQ-7 at Week 24 of the treatment period (Visit 5).
Dosing	• Participants will self-administer their first dose in the clinic and will continue to administer FF/UME/VI at approximately the same time each morning for the duration of the treatment period. Each subject will be instructed on the proper use of the ELLIPTA and will inhale once from the ELLIPTA each morning

Overview of Study Design and Key Features	
Time & Events	• Refer to Appendix 2: Schedule of Activities: Schedule of Activities
Treatment Assignment	• Eligible patients who meet the pre-defined criteria at screening (Visit 1) will enter into a 2-week run-in period. During the run-in period, the participants will continue their pre-screening inhaled medications for asthma (ICS+ LABA or ICS+LABA+ LAMA) until the day before Visit 2 without any change in regimen/dosage. • After completion of the run-in period, participants who meet pre-defined criteria at Visit 2 will be allocated to either FF/UMEC/VI 100/62.5/25 mcg (Group 1) or FF/UMEC/VI 200/62.5/25 mcg (Group 2) depending on the asthma control status with inhaled asthma therapy during the run-in period and initiate a 52-week treatment period.
Interim Analysis	• No statistical interim analysis requiring hypothesis test is planned. However, the data will be summarized when all participants (who have not withdrawn) have completed 24-week administration during treatment period and the CRF data up to Week 24 for all participants is locked. It will be used for a JNDA submission.

2.4. Statistical Hypotheses / Statistical Analyses

This study has no statistical hypotheses since this is an open-label non-randomised study.

3. PLANNED ANALYSES

3.1. Interim Analyses

No statistical interim analysis requiring any hypothesis tests is planned. However, the data will be summarized when all participants (who have not withdrawn) have completed 24-week administration of IP during the treatment period and the CRF data up to Week 24 for all participants is locked. It will be used for a JNDA submission.

Data up to week 24 (specifically, data up to the date of visit 5 (week 24) or the date of withdrawal before week 24 visit for a given subject) will be used for outputs (i.e., tables/figures). The definition of the cut-off date for the interim analysis will be the date of Visit 5 (Week 24) for the last enrolled participant in this study. As for the AE data to be included in interim analyses, please also refer to the definition of AE assessment window (11.3.2.1).

The interim planned primary analyses will be performed after the completion of the following sequential steps for this Clinical Data Interchange Standards Consortium [CDISC] study:

1. All participants have completed the 24-week administration during treatment period (except for the premature withdrawals) as defined in the protocol.
2. All required database cleaning activities have been completed and interim DBR for the 24-week during treatment period has been declared by Data Management (DM).

3. System Independent (SI) data to Study Data Tabulation Model (SDTM) data conversion has been completed by Conversion Service Provider at interim Source Data Lock (SDL).
4. Randomisation codes have been distributed according to RandAll NG procedures
5. Interim Database freeze (DBF) on interim SDTM datasets has been declared by DM.

3.2. Final Analyses

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

1. All participants have completed the study as defined in the protocol.
2. All required database cleaning activities have been completed and final DBR has been declared by Data Management (DM).
3. System Independent (SI) data to Study Data Tabulation Model (SDTM) data conversion has completed by Conversion Service at final Source Data Lock (SDL).
4. Final DBF on final SDTM datasets has been declared by DM.

Note: Randomisation codes had already been distributed in interim analyses.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Subjects	• All participants for whom a record exist on the study database, including pre-screened subjects that sign the informed consent document but do not complete a screening procedure (i.e., pre-screening failures) • This population will be used for the summary of "study populations" as study disposition	• Study Population
Screened	• All screened participants. • This population will be used for the summary of reasons for screening failures.	• Study Population
Enrolled	• All participants who are found to be eligible for the study based on the screening examination result. • This population will be used for the summary tables required by EudraCT.	• Study Population
Intent-To-Treat (ITT)	• All participants who take at least one dose of study treatment in the treatment period. Participants will be analyzed according to the treatment they actually received. • This population will be used for all safety and other analyses.	• Safety • Study Population • Other

Refer to Appendix 11: List of Data Displays which details the population used for each display.

4.1. Protocol Deviations

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

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan [1Aug2018 Version 3.0].

- Data will be reviewed prior to freezing the database to ensure all important deviations are captured and categorised on the protocol deviations dataset.
- Participants who received an incorrect treatment will be captured as an important protocol deviation. The incorrect treatment will be identified in eCRF (if "No" to the question "Did the subject receive the correct treatment?" then this participants will be regarded as having received an incorrect container).
- This dataset will be the basis for the summaries and listings of protocol deviations.

A separate listing of all inclusion/exclusion criteria deviations will also be provided. This 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

5.1.1. Interim Analyses

In interim analyses, only data until 24 weeks after first treatment will be used. This means the data after switching medication will NOT be included. Therefore, description in data displays will be the same as description in RandAll NG.

Treatment Group Descriptions for Interim Analyses			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order [1]
A	FF/UMEC/VI 100/62.5/25	FF/UMEC/VI 100/62.5/25	1
B	FF/UMEC/VI 200/62.5/25	FF/UMEC/VI 200/62.5/25	2

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.

Treatment comparisons will not be displayed.

If a given subject has incorrect study treatment during all period, then this subject will be analysed according to the treatment which he/she received. However, since it is uncertain whether a given subject has incorrect study treatment during all period (for 52 weeks) as of the timing of interim analyses, all analysis will be according to the allocated dose for interim analyses.

5.1.2. Final Analyses

In final analyses, two approaches for summaries will be used depending on summary tables.

5.1.2.1. Analyses by dose group

In principle, description in data displays will follow the patterns taking the treatment switching into account. All final analyses will use these descriptions below, except for summaries for "AE analyses by dose at the time of onset of the AE".This approach is based on both the allocated doses and status of treatment switch at Week 24. Note that the participants will be allocated to either FF/UMEC/VI 100/62.5/25 mcg or FF/UMEC/VI 200/62.5/25 mcg, and only the participants who are allocated to FF/UMEC/VI 100/62.5/25 mcg will be allowed to switch treatment to FF/UMEC/VI 200/62.5/25 mcg only at Week24. Therefore, treatment descriptions will be three as below table.

In this approach, summaries for total (overall) will be also presented.

Treatment Group Descriptions for Final Analyses by dose group				
RandAll NG		Switched treatment at Week 24	Data Displays for Reporting	
Code	Description	Description	Description	Order [1]
A	FF/UMEC/VI 100/62.5/25	No (FF/UMEC/VI 100/62.5/25 after week 24 or discontinued this study by week 24)	Only FF/UMEC/VI 100/62.5/25	1
A	FF/UMEC/VI 100/62.5/25	Yes (Switched to FF/UMEC/VI 200/62.5/25 at week 24)	FF/UMEC/VI 100/62.5/25 to FF/UMEC/VI 200/62.5/25	2
B	FF/UMEC/VI 200/62.5/25	N/A (Switched treatment will not be acceptable)	Only FF/UMEC/VI 200/62.5/25	3

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.

5.1.2.2. Analyses by dose the time of onset of the AE (by dose at AE)

"AE analyses by dose at the time of onset of the AE" will be planned in this study due to Japan regulatory authority requirement. In these analyses, the following descriptions will be used.

Treatment Group Descriptions for Final Analyses by dose at AE			
Dose at AE		Data Displays for Reporting	
	Description	Description	Order [1]
A	FF/UMEC/VI 100/62.5/25	FF/UMEC/VI 100/62.5/25	1
B	FF/UMEC/VI 200/62.5/25	FF/UMEC/VI 200/62.5/25	2

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.

In "by dose at AE" approach, the following rule will be applied.

- If a given subject is allocated to FF/UMEC/VI 100/62.5/25 at visit 2 and not switched at visit 5 then this subject will be handled as FF/UMEC/VI 100/62.5/25.
- If a given subject is allocated to FF/UMEC/VI 200/62.5/25 at visit 2 then this subject will be handled as FF/UMEC/VI 200/62.5/25.
- If a given subject is allocated to FF/UMEC/VI 100/62.5/25 at visit 2 and switched at visit 5 then this subject will be handled as FF/UMEC/VI 100/62.5/25 until the day before visit 5 (week 24 visit) and as FF/UMEC/VI 200/62.5/25 after the day of visit 5 (week 24 visit). This means AEs which occurred until the day before visit 5 (week 24 visit) will be summarized in FF/UMEC/VI 100/62.5/25 and AEs which occurred after the day of visit 5 (week 24 visit) will be summarized in FF/UMEC/VI 200/62.5/25.

Treatment comparisons will not be displayed.

If a given subject has incorrect study treatment during all period, then this subject will be analysed according to the treatment which he/she received. This will be identified as all answers will be "No" to the question "Did the subject receive the correct treatment?" for all visits on eCRF.

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 (except any assessments from unscheduled visit at the same date as Day1) are assumed to be taken prior to first dose and used as baseline.

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

5.3. Multicentre Studies

In this multicentre local study, enrolment will be presented by investigative site.

5.4. Examination of Covariates, Other Strata and Subgroups

5.4.1. Covariates and Other Strata

Any covariates and other strata will not be used in descriptive summaries and statistical analyses.

Subgroup analyses will not be planned in this study.

5.5. Multiple Comparisons and Multiplicity

Since this study does not plan efficacy analyses, multiple comparisons and multiplicity will not be applied.

5.6. 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
11.3	Appendix 3: Assessment Windows
11.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
11.5	Appendix 5: Data Display Standards & Handling Conventions
11.6	Appendix 6: Derived and Transformed Data
11.7	Appendix 7: Reporting Standards for Missing Data

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the 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. All outputs unless specified otherwise will be produced for the interim analysis and final analysis.

6.1.1. Subject Disposition

The overall subject disposition as well as the reason for withdrawal will be summarized for the ITT population, including the number and percentage of participants in each dose group and total. In interim analysis, "completed" means completion of Visit 5 (Week 24 visit).

The number and percentage of participants who completed the study treatment as well as the number who stopped the study treatment prior to the end of the study will be summarized, along with the reasons for discontinuation of the study treatment.

The reasons for Screen Failure or Run-in Failure will be summarized for the Screened Population for interim analysis only. Listings of failures prior to treatment will be generated.

The number and percentage of participants in each dose group and total will be summarized by status (entered, completed or withdrawn) at each epoch (run-in period, treatment period and follow-up period). In interim analysis, "completed" means completion of Visit 5 (Week 24 visit).

Using All Subjects, the number of participants in each population (Screened, Enrolled, ITT) will be summarized by dose group and total.

The number and percentage of participants at each center and within each country will be summarized. Note that this study includes only Japan as country.

6.1.2. Protocol Deviation

The number and percentage of participants with important protocol deviations determined by the study team will also be summarized. Listing for important protocol deviations will be prepared as well.

Listing will be provided for inclusion / exclusion criteria deviation record.

6.1.3. Demographic and Baseline Characteristics

Each of the following types of data will be summarized by dose group and total:

- Demographic data (age, sex, ethnicity, weight, height, body mass index (BMI), race)
- Duration of asthma
- Asthma medical history questionnaire
- Smoking history (smoking status of non-smoker or former smoker, and pack years for former smokers)
- Exacerbation history
- Cardiovascular history / risk factors and family history of cardiovascular risk factors
- ACQ-6 scores at Visit 1
- Pulmonary function (FEV_1, FVC, %predicted FEV_1)

Note: % predicted FEV1 will be derived. See Section 11.6.2.

6.1.4. Prior and Concomitant Medications

Summaries will be provided for the asthma medications before study treatment, as well as summaries for both asthma and non-asthma medication during the treatment period and during follow-up period. A total column will be included for the all summaries. Listings will be provided for the asthma and non-asthma concomitant medications.

Non-Asthma medication tables will report by Anatomical Therapeutic Chemical (ATC) level 1 and ingredient. Asthma medication tables will report by respiratory medication class (RMC) and ingredient.

Multi-ingredient medications will be presented according to their combination ATC classification rather than the classification of the ingredients.

6.1.5. Treatment Compliance

Treatment compliance will be assessed during the treatment period by dose group and total.

For the treatment period, the actual total number of doses received by each subject will be calculated as the sum of (dose counter start value – dose counter stop value) over all inhalers dispensed to the subject during the treatment period and returned prior to or at the EOT/EW visit, and percentage compliance will be calculated as follows:

$$Treatment\ \ Compliance = \frac{total\ number\ of\ \ doses\ received}{treatment\ stop\ date - treatment\ start\ date + 1} \times 100.$$

In interim analysis, treatment compliance will be calculated based on data until the day before visit 5 (i.e., treatment stop date will be replaced with the day before visit 5). Details on the derivations are provided in Section 11.6.2.

7. EFFICACY ANALYSES

This is an open-label study and the efficacy will be assessed in an exploratory manner. Therefore, no efficacy endpoint is defined and the efficacy will be assessed as other endpoints.

8. SAFETY ANALYSES

The safety analyses will be based on the ITT population, unless otherwise specified. All outputs unless specified otherwise will be produced for the interim analysis and final analysis.

8.1. Extent of Exposure

Overall extent of exposure to study treatment will be summarized in increments of 4 weeks for ≥1 day, ≥4 weeks, ≥8 weeks, ≥12 weeks, ≥16 weeks, ≥20 weeks, ≥24 weeks, ≥28 weeks, ≥32 weeks, ≥36 weeks, ≥40 weeks, ≥44 weeks, ≥48 weeks, ≥52 weeks, in addition to providing summary statistics and total treatment exposure (person-year).

8.2. 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.

All AEs will be classified using the standard GSK Medical Dictionary for Regulatory Activities (MedDRA) dictionary, and grouped by SOC and PT, unless otherwise stated. The investigator will evaluate all AEs with respect to seriousness, severity, and causality.

The tabular summary for each type of AE listed below will include the number of participants who reported at least one event, and percentage of participants who reported at least one AE (incidence) for each SOC (where applicable), each PT, and overall. By default, adverse events will be sorted by MedDRA SOCs, in descending order from the SOC with the highest total incidence (i.e., summed across all dose groups) for any adverse event within the class, to the SOC with the lowest total incidence. If the total incidence for any two or more adverse events is equal, the events will be presented in alphabetical order. Only SOCs with observed AE PTs will be presented. Repeat sort order for MedDRA PTs within each SOC.

In principle, all safety analyses will be provided by dose group and total. However, due to Japan regulatory authority requirement, AE analyses by dose at the time of onset of the AE will be prepared in final analyses of this study. Note that dose at the time of onset of the AE will be decided by allocated dose even if a given subject has incorrect study treatment in certain period (but not during all period). If a given subject has incorrect study treatment during all period, then this subject will be analysed according to the treatment which he/she received. In interim analyses, selected tables will be provided. Please refer to Section 11.11.5.

Each type of the following will be summarized for both approaches (i.e., by dose group and total, by dose at the time of onset of the AE)

- AE overview during treatment period
- All AEs during treatment period (by SOC and PT; by SOC and PT and maximum severity)
- Drug related AEs during treatment period (by SOC and PT; by SOC and PT and maximum severity)
- Serious AEs during treatment period (by SOC and PT)
- AEs resulting in withdrawal from study (by SOC and PT)

- AEs of Special Interest during treatment period (by SOC and PT)
- Most Common Adverse Events during treatment period (3% or More of subjects in Any Treatment Group) (by PT)

The following AE summaries will be provided only by dose group and total.

- All AEs adjusted for exposure (per thousand person years) during treatment period (by SOC and PT)
- All AEs during follow-up period (by SOC and PT)
- Drug related AEs adjusted for exposure (per thousand person years) during treatment period (by SOC and PT)
- Drug related AEs during treatment period and follow-up period (by SOC and PT)
- All AEs for week 0-12, week 13-24, week 25-36 and week 37-52 during treatment period (by SOC and PT)
- All AEs for week 0-24, week 25-52 during treatment period (by SOC and PT)
- Serious AEs adjusted for exposure (per thousand person years) during treatment period (by SOC and PT)
- AEs of Special Interest adjusted for exposure (per thousand person years) during treatment period (by SOC and PT)
- Common Non-Serious AEs by SOC and PT during treatment period (Number of Subjects and Occurrences) (5% or More of subjects in Any Treatment Group)
- Summary of Serious Adverse Events by System Organ Class and Preferred Term during treatment period (Number of Participants and Occurrences)
- Major Adverse Cardiac Events
- Serious Drug Related Adverse Events during treatment period (for PLS, final analysis only)
- Non-Serious Drug Related Adverse Events during treatment period (for PLS, final analysis only)

The following AE listings will be provided. These listing include information of dose group, not dose at AE.

- All AEs, Fatal serious AEs, Non-Fatal AEs, AEs leading to permanent discontinuation of study treatment or withdrawal from study
- Relationship of AE SOCs, PTs and Verbatim text
- Reasons for considering as a serious AE

8.3. 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. The details of the planned displays are provided in Appendix 11: List of Data Displays.

Adverse Events of Special Interest (AESI) are those AEs associated with the known pharmacological action of ICSs and/or LAMAs and/or LABAs, regardless of whether the AE has been specifically described for FF and/or UMEC and/or VI. AESI groupings are compiled in one of two ways: where SMQs (pre-defined lists of MedDRA PTs) are available from MedDRA for specific AESIs, these are used; and where SMQs are not available, a GSK-defined list of all relevant MedDRA PTs is used.

For FF/UMEC/VI, the special interest groups are: adrenal suppression, corticosteroid-associated and antimuscarinic-associated ocular effects, decreased bone mineral density and associated fractures, hypersensitivity, pneumonia, LRTI excluding pneumonia, local steroid effects, effects on potassium, tremor, CV effects, effects on glucose, asthma/bronchospasm, anticholinergic syndrome. Gastrointestinal obstruction, urinary retention.

Table 1 presents the special interest AE groups for FF, UMEC and VI.

Table 1 AESI definitions

Special Interest AE Group	Special Interest AE Subgroup	PTs for Inclusion
Cardiovascular effects*	Cardiac arrhythmia	Cardiac arrhythmia (SMQ) , excluding congential and neonatal arrhythmias (SMQ)
	Cardiac failure	Cardiac Failure (SMQ)
	Cardiac ischaemia	Ischaemic Heart Disease (SMQ)
	Stroke	Central nervous system haemorrhages and cerebrovascular conditions (SMQ)
	Hypertension	Hypertension (SMQ)
Pneumonia*	Pneumonia	Infective Pneumonia (Narrow SMQ)
LRTI excluding infective pneumonia SMQ*	LRTI excluding infective pneumonia SMQ	Selected PTs

Special Interest AE Group	Special Interest AE Subgroup	PTs for Inclusion
Decreased bone mineral density and associated fractures	Decreased bone mineral density and associated fractures	Osteoporosis/Osteopenia (SMQ) Selected PTs
Hypersensitivity*	Hypersensitivity	Hypersensitivity (SMQ) Angioedema (SMQ) Anaphylactic reaction (SMQ)
Anticholinergic Syndrome*	Anticholinergic syndrome	Anticholinergic Syndrome (SMQ)
Gastrointestinal obstruction*	Gastrointestinal obstruction	Gastrointestinal obstruction (SMQ)
Adrenal Suppression	Adrenal Suppression	Selected PTs
Antimuscarinic ocular effects* / Corticosteroid Associated Eye Disorders	Glaucoma (antimuscarinic / corticosteroid)	Glaucoma (SMQ)
	Cataracts (corticosteroids)	Lens disorders (SMQ)
Effects on Glucose	Effects on Glucose	Hyperglycaemia/new onset diabetes mellitus (SMQ)
Local steroid effects	Local steroid effects	Selected PTs
Urinary retention*	Urinary retention	Selected PTs
Effects on potassium	Effects on potassium	Selected PTs
Tremor	Tremor	Selected PTs
Asthma/Bronchospasm for Asthma-related intubations and deaths	Asthma/Bronchospasm for Asthma-related intubations and deaths	Asthma/bronchospasm (SMQ)
Dry mouth / Drying airway secretions*	Dry mouth / Drying airway secretions	Selected PTs (narrow & broad focus)
*: of interest for UMEC .		

Adverse events of special interest will be summarized in the same manner outlined in Section 8.2 for overall AEs.

8.4. MACE

The MACE (Major Adverse Cardiac Events) endpoint will be analyzed using broad and narrow definitions.

The Broad MACE will be defined as follows:

- Cardiac Ischaemia Special Interest AE Subgroup (Ischaemic Heart Disease SMQ) including fatalities,
- Stroke Special Interest AE Subgroup (Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ) including fatalities

The narrow MACE definition will include only the PTs of "myocardial infarction" and "acute myocardial infarction" in place of the Cardiac Ischaemia Special Interest AE subgroup.

8.5. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Hematology laboratory tests, Urinalysis, and liver function tests will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 11: List of Data Displays.

Clinical laboratory will be measured at visit 1 (screening visit), 4 (Week 12), 5 (Week 24), 7 (Week 52) or EW. and will be summarized by dose group.

Raw value and change from baseline for laboratory data will be summarized by dose group and total for each visit.

Shifts from baseline relative to the normal range will be also summarized by dose group and total for each visit.

The number of participants with worst case chemistry or hematology will be summarized by test and category. The categories for normal range are: To Low, To Normal or No Change, To High. The categorization is determined by comparing the baseline category to the worst case post-baseline category. The determination of the worst case post-baseline takes into account both planned and unscheduled assessments. The percentages are based on the number of participants in the dose group with data for the test post-baseline. Participants with missing baseline value are to be assumed to have normal/within range baseline value. Note that if a subject has both a decrease 'To Low' and an increase 'To High', then the subject is counted in both the 'To Low' and 'To High' categories, so the percentages may not add to 100%.

The number of participants with worst case protein (category: NEG, TRA, 1+, 2+, 3+) or occult blood (category: NEG, TRA, 1+, 2+, 3+) urinalysis results will be summarized by test and category. The categories for worst case are: No Change/Decresed, Any Increase, Increase to TRA, Increase to 1+, Increase to 2+, Increase to 3+. The categorization is determined by comparing the baseline category to the worst case post-baseline category. The determination of the worst case post-baseline takes into account both planned and unscheduled assessments. The percentages are based on the number of participants in the dose group with data for the test post-baseline. Participants with missing baseline value are to be assumed to have normal/within range baseline value.

8.6. 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.

8.6.1. Vital signs

Vital signs will be measured at every clinical visit and will be summarized by dose group and total.

Raw value and change from baseline for Vital signs will be summarized by dose group and total for each visit.

8.6.2. ECG

12-lead ECGs are measured at Visit 1, 3, 5 and 7, and at Early Withdrawal visit. The ECG measurements of interest are QTc (F), heart rate, and PR interval. All ECG data present in the database will be considered valid and will be reported (even if the ECG had a technical error).

Raw value and change from baseline for ECG values will be summarized by dose group and total for each visit.

A 'maximum post-baseline' QTc (F), PR interval, and heart rate value will be derived as the maximum on-treatment value recorded at any scheduled, unscheduled, or EW visit after the start of study treatment.

QTc (F) values (including 'maximum post-baseline') will be categorized as follows: ≤450msec, >450 to ≤ 480msec, >480 to ≤500msec, >500 to ≤530msec and >530msec. Change from baseline QTc (F) values (including change to 'maximum post baseline') will be categorized as follows: ≤-60msec, >-60 to ≤-30msec, >-30 to ≤0msec, >0 to ≤30msec, >30 to ≤60msec, and >60msec.

An 'any time post-baseline' ECG interpretation will be derived as the worst on-treatment interpretation recorded at a scheduled, unscheduled, or EW visit after the start of study treatment. The worst case post-baseline is defined as:

- 'Abnormal' if any assessment during treatment period is evaluated as 'Abnormal'
- 'Unable to evaluate' if all assessments during treatment period are 'Unable to evaluate'
- 'Normal' if any assessment during treatment period is evaluated as 'Normal' and there are no assessments evaluated as 'Abnormal' during treatment period

8.6.3. Pregnancy

Any pregnancies reported during the study will be summarized in case narratives. Any pregnancy complication or elective termination of a pregnancy for medical reasons will be recorded as an AE or SAE and included in summaries and listings of AEs/SAEs.

9. OTHER ANALYSES

9.1. Other Analyses

This is an open-label study and the efficacy will be assessed in an exploratory manner. Therefore, no efficacy endpoint is defined and the efficacy will be assessed as other endpoints. No statistical analyses (using statistical models or tests) will be planned in this RAP. Only summary tables or listings will be provided.

9.1.1. Overview of Planned Other Analyses

The other analyses will be based on "ITT" population, unless otherwise specified. All outputs unless specified otherwise will be produced for the interim analysis and final analysis.

Summary statistics for absolute value and change from baseline will be provided for following endpoints at visit 2 (Week 0), 5 (Week 24) and 6 (Week 52) by dose group and total.

- Trough Forced Expiratory Volume in 1 second (FEV_1)
- ACQ-7 total score
- St. George's Respiratory Questionnaire (SGRQ) total score
- Asthma Quality of Life Questionnaire (AQLQ) total score

ACQ-6 will be measured at visit 1 for eligibility criteria. ACQ-6 will not be summarized in other analyses, but in demographic and baseline characteristics, see Section 6.1.3.

Summaries of all-cause unscheduled asthma related healthcare resource utilization over 52 weeks of the treatment period will be provided in only final analysis. Total below means total number of contacts across all participants.

- Unscheduled healthcare utilization (Yes or No)
- Number of telephone call (n, 0, 1, 2, 3, >3, Total)
- Number of home visit (day) (n, 0, 1, 2, 3, >3, Total)
- Number of home visit (night) (n, 0, 1, 2, 3, >3, Total)
- Number of physician office/practice visits (n, 0, 1, 2, 3, >3, Total)
- Number of urgent care / outpatient clinic visits (n, 0, 1, 2, 3, >3, Total)
- Number of emergency room visits (n, 0, 1, 2, 3, >3, Total)
- Number of inpatient hospitalisation days (ICU) (n, 0, 1, 2, 3, >3, Total)
- Number of inpatient hospitalisation days (General ward) (n, 0, 1, 2, 3, >3, Total)
- Was this contact due to an exacerbation (Yes or No)

Summary of annualized rate of severe asthma exacerbations and annualized rate of moderate/severe asthma exacerbations will be provided (only the number of participants and calculated annualized rate will be provided for this summary). Annualized rate for a given dose group will be calculated as follows, but only at final analysis:

- Summation of (total number of exacerbations) for all participants in a given dose group (or all participants for total) is divided by summation of ((date of Visit 7 / EOT visit or EW visit – treatment start date +1) / 365) for all participants in a given dose group (or all participants for total).

As for asthma exacerbations, following information will be provided.

- Number of events
    - Hospitalization
    - Emergency room visit
    - Systemic/oral corticosteroid use
    - Outcome (Resolved, Fatal or Not Resolved)
    - Duration (days), which will be calculated as Date of Outcome – Date of Onset + 1. If Outcome is Not resolved, then duration will be missing
- Number of participants with events (0, 1, 2, >2)
    - Severe
        - Hospitalization
        - Emergency room visit
        - Systemic/oral corticosteroid use
    - Moderate

10. REFERENCES

Asthma Control Questionnaire, Background, Administration and Analysis, April, 2008.

Asthma Quality of Life Questionnaires (AQLQ, AQLQ(S), MiniAQLQ and Acute AQLQ), Background, Administration and Analysis, June, 2005.

GlaxoSmithKline Document Number 2016N305271_02 Study 207236, A Phase III, 52-week, Open-label Study to Evaluate Long-term Safety of Fixed Dose Combination Therapy Fluticasone Furoate/Umeclidinium Bromide/Vilanterol Trifenatate in Japanese Patients with Asthma. Effective Date: 25-OCT-2017.

Implementing GLI-2012 regression equations, July 16, 2015

Philip H. Quanjer et al, Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations, Eur Respir J 2012; 40: 1324–1343

St George's Respiratory Questionnaire (SGRQ) Manual, *Version 2.3 June, 2009*

11. APPENDICES

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

Per Protocol Population is not defined in this study.

11.2. Appendix 2: Schedule of Activities

11.2.1. Protocol Defined Schedule of Events

Procedure	Pre-screen	Run-in	Treatment period							Follow-up
Visit	0	1 Screening	2 Baseline	3	4	5	6	7 End of Treatment (EOT)	Early Withdrawal (EW)	Safety follow-up contact
Day	-28 to -14	-14	1	29	85	169	253	365		
Week	-4 to -2	-2	0	4	12	24	36	52		
Window		-3		-5/+2d	-5/+2d	-5/+2d	-5/+2d	-5/+2d		
Informed consent[1]	X									
Genetics/Pharmacogenetic informed consent[2]	X									
Inclusion and exclusion criteria		X	X							
Demography	X									
Past and current medical conditions including asthma history[3] and exacerbation history		X								
Smoking history and status		X								
Concomitant medication review		X	X	X	X	X	X	X	X	X
Allocation/registration[4]			X							
Register visit in IRT (RAMOS NG)[5]	X	X	X	X	X	X	X	X	X	X
Safety Assessment										
Physical examination		X				X		X	X	
Weight/height		X								
Adverse events			X	X	X	X	X	X	X	X
Serious adverse events	X	X	X	X	X	X	X	X	X	X
Vital signs (blood pressure and pulse rate)		X	X	X	X	X	X	X	X	
ECG		X		X		X		X	X	
Hematology and clinical chemistry		X			X	X		X	X	
Urinalysis		X			X	X		X	X	
Serum pregnancy test		X[6]			X[6]	X[6]		X[6]	X[6]	
Urine pregnancy test [6]			X	X			X			

Procedure	Pre-screen	Run-in	Treatment period							Follow-up
Visit	0	1 Screening	2 Baseline	3	4	5	6	7 End of Treatment (EOT)	Early Withdrawal (EW)	Safety follow-up contact
Day	-28 to -14	-14	1	29	85	169	253	365		
Week	-4 to -2	-2	0	4	12	24	36	52		
Window		-3		-5/+2d	-5/+2d	-5/+2d	-5/+2d	-5/+2d		
Other Assessment										
ACQ[7]		X[8]	X[9]			X[9]		X[9]	X[9]	
SGRQ[7]			X			X		X	X	
AQLQ[7]			X			X		X	X	
Pre-dose spirometry [10]			X			X		X	X	
Moderate/severe asthma exacerbation			X	X	X	X	X	X	X	X
Genetics/Pharmacogenetic sampling [11]			X							
Dispense paper Medical Problems/Medications Taken worksheet	X	X	X	X	X	X	X	X	X	
Review paper Medical Problems/Medications Taken worksheet		X	X	X	X	X	X	X	X	X
Healthcare resource utilization			X	X	X	X	X	X	X	
Dispense investigational product			X	X	X	X	X			
Collect investigational product				X	X	X	X	X	X	
Dispense salbutamol (as required)		X	X	X	X	X	X			
Collect salbutamol (as required)			X	X	X	X	X	X	X	

1. The Informed Consent Form (ICF) must be signed before any study procedures, including medication cessation.
2. Genetics/Pharmacogenetic research consent may be obtained at the same time as the study Informed Consent and must be obtained prior to obtaining a Genetics/pharmacogenetic blood sample.
3. The assessment of asthma history will include: the age of the subject when they were first provided with an inhaler for asthma; completion of an asthma medical history questionnaire (a copy of this questionnaire and instructions for its use can be found in the SRM).
4. Subjects must not be allocated prior to confirming their eligibility to participate in the study.
5. The IRT will be used for allocation, and study treatment supply management (Please refer to the RAMOS NG IRT manual and SRM for more information).
6. Assessments are only to be conducted in females of reproductive potential.
7. Assessment(s) to be completed before any study procedures .Study treatment should be administered at the same time of day each applicable clinic visit,
8. Assessment to be conducted by using ACQ-6
9. Assessment to be conducted by using ACQ-7

10. Spirometry to be performed after withholding rescue medication for at least 6 hours and prior to taking the morning dose of study treatment. Pre-dose spirometry assessments should be performed at the same time of day at each applicable visit.
11. Pharmacogenetic sample may be drawn any time from Visit 2 onwards.

ACQ: Asthma Control Questionnaire, AQLQ: Asthma Quality of Life Questionnaire, IRT: Interactive Response Technology, SGRQ: St. George's Respiratory Questionnaire

11.3. Appendix 3: Assessment Windows

11.3.1. Clinical visits

Clinic visits are scheduled to take place as specified in the protocol. Measurements outside visit windows will not be excluded from analyses on any population.

For all clinic visits, nominal visits will be used for reporting.

All unscheduled visits will be included in listings.

11.3.2. Definitions of Assessment Windows for Adverse Events in Treatment Period

Definition of assessment windows is different among dose groups. Day 1 is defined as the study treatment start day. Section 11.3.2.1 and Section 11.3.2.2 are applicable only AE summaries by period (i.e., All AEs for week 0-12 and week 13-24 during treatment period in interim analysis, and All AEs for week 0-12, week 13-24, week 25-36 and week 37-52 during treatment period in final analysis). Section 11.3.2.3 is applicable for the approach "by dose at AE".

11.3.2.1. In Interim Analyses

In interim analyses, the table below will be applied (i.e., data up to the day before visit 5 (week 24 visit) will be used for AE/SAE related analyses).

Analysis Window		Analysis Timepoint
Beginning Timepoint	Ending Timepoint	
Day 1	Day 84	Week 0-12
Day 85	The day before visit 5 (week 24 visit) Or Day 168 (only for participants who withdraw early)	Week 13-24

Note that the data except for AE/SAEs up to the day OF visit 5 (week 24 visit) will be used in interim analyses. This means data except for AE/SAEs (e.g., clinical laboratory) will include visit 5 (week 24 visit), but data for AE/SAEs will not include the day of visit5 (week 24 visit) in interim analyses.

11.3.2.2. In Final Analyses

For treatment group of "only FF/UMEC/VI 100/62.5/25" and "only FF/UMEC/VI 200/62.5/25", the table below will be applied (see Section 11.5.1 for treatment group description).

Analysis Window		Analysis Timepoint
Beginning Timepoint	Ending Timepoint	
Day 1	Day 84	Week 0-12
Day 85	Day 168	Week 13-24
Day 169	Day 252	Week 25-36
Day 253	Day 365 Or The day of visit 7 (week 52 visit) if this is later than Day 365	Week 37-52
Day 1	Day 168	Week 0-24
Day 169	Day 365 Or The day of visit 7 (week 52 visit) if this is later than Day 365	Week 25-52

For treatment group of "FF/UMEC/VI 100/62.5/25 to FF/UMEC/VI 200/62.5/25", the table below will be applied (see Section 5.1 for treatment group description). The reason to use separate analysis window for "FF/UMEC/VI 100/62.5/25 to FF/UMEC/VI 200/62.5/25" is to consider the day of switched treatment (i.e. the day of week 24).

Analysis Window		Analysis Timepoint
Beginning Timepoint	Ending Timepoint	
Day 1	Day 84	Week 0-12
Day 85	The day before visit 5 (week 24 visit)	Week 13-24
The day of visit 5 (week 24 visit)	Day 252	Week 25-36
Day 253	Day 365 Or The day of visit 7 (week 52 visit) if this is later than Day 365	Week 37-52
Day 1	The day before visit 5 (week 24 visit)	Week 0-24
The day of visit 5 (week 24 visit)	Day 365 Or The day of visit 7 (week 52 visit) if this is later than Day 365	Week 25-52

11.3.2.3. By dose at the time of onset of the AEs (by dose at AE)

For treatment group of "only FF/UMEC/VI 100/62.5/25" and "only FF/UMEC/VI 200/62.5/25", the approach "by dose at AE" will summarized AEs during treatment period as each dose.

For treatment group of "FF/UMEC/VI 100/62.5/25 to FF/UMEC/VI 200/62.5/25", the table below will be applied for an approach "by dose at AE" analyses.

Analysis Window		By dose at AE
Beginning Timepoint	**Ending Timepoint**	
Day 1	The day before visit 5 (week 24 visit)	As FF/UMEC/VI 100/62.5/25
The day of visit 5 (week 24 visit)	Day 365 Or The day of visit 7 (week 52 visit) if this is later than Day 365	As FF/UMEC/VI 200/62.5/25

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

11.4.1. Study Phases

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

Study Phase	Definition
Screening/Run-In period	Visit 1 date ≤ Assessment Date/Time < Date of study treatment start date
Treatment period	Study Treatment Start Date ≤ Date ≤ Date of Visit7/EOT or EW
Follow-up period	Date > Date of Visit7/EOT or EW

11.4.1.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is before study treatment start date
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.

11.4.2. 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.

NOTES:

- If the study treatment stop date is missing, then the AE will be considered to be On-Treatment.

11.5. Appendix 5: Data Display Standards & Handling Conventions

11.5.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	¥¥uk1salx00175.corpnet2.com¥
HARP Compound	Primary (interim) analysis: ¥arenv¥arprod¥gsk2834425¥mid207236¥primary_01 Final analysis: ¥arenv¥arprod¥gsk2834425¥mid207236¥final_01
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2& ADaM IG Version 1.0).	
Generation of RTF Files	
• RTF files will not be generated	

11.5.2. Reporting Standards

General

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

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

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

Unscheduled Visits
• Unscheduled visits will not be included in summary tables and/or figures except as part of a '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.	

11.6. Appendix 6: Derived and Transformed Data

11.6.1. General

Multiple Measurements at One Analysis Time Point
• If there are two values within a time window, 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 < Treatment Start Date → Study Day = Ref Date – Treatment Start Date
  • Ref Data ≥ Treatment Start Date → Study Day = Ref Date – (Treatment Start Date) + 1

Example of Handling the Incorrect Treatment and Dose at the Timing of Onset of the AE

Here are the examples 1- 3 which a given subject had the incorrect treatment in certain period or all periods in treatment period (week 0 to week 52). It is assumed that all participants here complete study (i.e., do not withdraw).

Example	1			2			3		
Dose group	FF/UMEC/VI 100/62.5/25			FF/UMEC/VI 100/62.5/25 to FF/UMEC/VI 200/62.5/25			FF/UMEC/VI 100/62.5/25		
allocated dose at week0	FF/UMEC/VI 100/62.5/25			FF/UMEC/VI 100/62.5/25			FF/UMEC/VI 200/62.5/25		
Switch treatment at week24	No			Yes			No		
Plan dose/ Actual dose/ dose at AE	Plan	Actual	dose at AE	Plan	Actual	dose at AE	Plan	Actual	dose at AE
week0 -4	FF100	FF100	FF100	FF100	FF100	FF100	FF200	FF100	FF100
week4 - 12	FF100	FF100	FF100	FF100	FF200	FF100	FF200	FF100	FF100
week12 - 24	FF100	FF100	FF100	FF100	FF100	FF100	FF200	FF100	FF100
week24 - 36	FF100	FF100	FF100	FF200	FF200	FF200	FF200	FF100	FF100
week36 - 52	FF100	FF200	FF100	FF200	FF100	FF200	FF200	FF100	FF100

Example 1 is the case that a given participant was allocated FF/UMEC/VI 100/62.5/25 at week0 and not switch the study treatment at week24, but had incorrect treatment (i.e., FF/UMEC/VI 200/62.5/25) at week 36 to 52. Therefore, as described in Section 5.1 and Section 8.2, dose group for this participant will be FF/UMEC/VI 100/62.5/25, and AE at week 36 – 52 will be handled as AE at FF/UMEC/VI 100/62.5/25 for dose at AE analyses.

Example 2 is the case that a given participant was allocated FF/UMEC/VI 100/62.5/25 at week0 and switched the study treatment at week24, but had incorrect treatment (i.e., FF/UMEC/VI 200/62.5/25 at week 4-12 and FF/UMEC/VI 100/62.5/25 at week 36-52) at two periods. Therefore, as described in Section 5.1 and Section 8.2, dose group for this participant will be FF/UMEC/VI 100/62.5/25 to FF/UMEC/VI 200/62.5/25, and AE at week 4 – 12 will be handled as AE at FF/UMEC/VI 100/62.5/25 and AE at week 36 – 52 will be handled as AE at FF/UMEC/VI 200/62.5/25 for dose at AE analyses.

Example 3 is the case that a given participant was allocated FF/UMEC/VI 200/62.5/25 at week0 and not switch the study treatment at week24, but had incorrect treatment (i.e., FF/UMEC/VI 100/62.5/25) during all periods. This participant HAD incorrect treatment during all periods. Therefore, as described in Section 5.1 and Section 8.2, dose group for this participant will be FF/UMEC/VI 100/62.5/25, and AE at any time will be handled as AE at FF/UMEC/VI 100/62.5/25 for dose at AE analyses.

11.6.2. Study Population

Demographics
Age

• Age will be calculated based on the Pre-Screening Visit date (or Screening, if pre-screening not performed).
• Birth date will be imputed as follows:
  ○ Any participant with a missing day and month will have this imputed as '30th June'.
  ○ All participants with imputed age of 17 or 18 years will be source data verified, and presence / absence of protocol deviation on the inclusion criteria #1 will be taken into consideration in the derivation for the analysis variable age.
• Birth date will be presented in listings as 'YYYY'.

Age Category

• Age categories (unless otherwise specified) are based on age at Pre-screening and are defined as:
  ○ 18 to < 65
  ○ 65 to <75 years
  ○ 75 to <85 years
  ○ ≥ 85 years
• Age categories in age range summary for EudraCT are based on age at Pre-screening and are defined as:
  ○ Adolescents (12-17 years)
  ○ Adult (18-64 years)
  ○ >=65-84 years
  ○ >=85 years

Body Mass Index (BMI)
○ Calculated as **Weight (kg) / Height (m)^2**
Cardiovascular History and Risk Factor

Cardiovascular history and risk factors will be assessed at Visit 1. Participants with one or more of the following terms recorded as either current or past medical conditions at Visit 1 is considered to have cardiovascular history/risk factors:
• Cardiovascular history
  • arrhythmia,
  • congestive heart failure,
  • coronary artery disease,
  • myocardial infarction,
  • cerebrovascular accidents,
• Cardiovascular risk factors
  • hypertension,
  • diabetes mellitus
  • hypercholesterolemia.

Treatment Compliance

- The actual total number of doses received by each participant will be calculated as the sum of (dose counter start value – dose counter stop value) over all inhalers dispensed to the participant during the treatment period, and percentage treatment compliance will be calculated as described in Section 6.1.5.

  If a dose counter start count is missing then it will be assumed to be 30 for the Ellipta DPI. If a dose counter stop value is missing then number of doses received will be set to missing for that container.

  Treatment compliance will be based only on the returned devices prior to or at end of study/early withdrawal visit that were dispensed during the treatment period.

- Overall compliance will be categorized as follows:
  < 50 %
  ≥50 % to < 80 %
  ≥80 % to < 95 %
  ≥95 % to ≤105 %
  >105 % to ≤120 %
  >120 %.

- If a participant receives a treatment other than the allocated treatment during the study, the compliance will still be calculated using data from all containers received and overall exposure start and stop dates
- In interim analysis, treatment compliance will be calculated based on data until the day before visit 5 (i.e., treatment stop date will be replaced with the day before visit 5).
- One dose per one day will be received in this study.

Derivation of Complete for Study Disposition in Interim Analysis

- In interim analysis, "completed" means completion of Visit 5 (Week 24 visit).
- If the response to the question "Did the subject fail to complete this phase of the study?" is "No" in eCRF, then this participant will be regarded as "completed" in interim analysis.

Derivation of % predicted FEV_1

- % predicted FEV_1 will be derived according to [Implementing GLI-2012 regression equations, July 16, 2015].

$$\% \text{ predicted FEV1} = (\text{measured FEV1 value} / M) \times 100$$

$$M = \exp(a_0 + a_1 \times \ln(\text{Height}) + a_2 \times \ln(\text{Age}) + a_6 + \text{Mspline})$$

Note: The integer value of calculated Age will be used in this study.

Note: ln() = natural log transformation.

Note: M is the predicted value of FEV_1.

Note: Since this study includes only Japanese participants, a_3 to a_5 are not used in this study. See Philip H. Quanjer et al (Philip, 2012) more detail.

- Coefficients of M

Derivation of % predicted FEV_1

Different coefficients of M need to be used for males and females.

	Coefficients of M in males	Coefficients of M in females
a_0	-10.3420	-9.6987
a_1	2.2196	2.1211
a_2	0.0574	-0.0270
a_6	-0.0708	-0.0708

- Mspline

Different Msplines need to be used depending on a participant's age and sex.

For 18-24 years, Msplines below will be used. These values come from "lookup tables" described in [Implementing GLI-2012 regression equations, July 16, 2015].

Age	Mspline in males	Mspline in females
18	0.1924	0.1785
19	0.2029	0.1823
20	0.2081	0.1839
21	0.2091	0.1841
22	0.2071	0.1832
23	0.2030	0.1812
24	0.1970	0.1785

For 25-95 years, Mspline will be calculated by using the formula below and coefficients.

$Mspline = b_0 + b_1*(Age/100) + b_2*(Age/100)^2 + b_3*(Age/100)^3 + b_4*(Age/100)^4 + b_5*(Age/100)^5$

	Coefficients of Mspline in males	Coefficients of Mspline in females
b_0	0.3901	0.0552
b_1	-1.0579	1.6029
b_2	1.4743	-6.4845
b_3	-2.1077	10.2723
b_4	-0.1215	-9.8630
b_5	0.8873	3.8802

11.6.3. Safety

Adverse Events
Adverse Event Rate
Event rate per thousand person-years will be displayed for AE data in separate tables as listed in Section 11.11.5 and Section 11.11.6. Event rate per thousand person-years will be calculated as the number of events x 1000 divided by the total participant exposure during the time-period of interest (i.e., during treatment period).
AE'S OF Special Interest
Adverse events of special interest have been defined as AEs which have specified areas of interest. These consist in groupings of preferred terms based on the MedDRA dictionary version used in each reporting effort. Subgroups may be defined, based on relevant combination of preferred terms, or on Standardized MedDRA queries (SMQ).

11.6.4. Other

Asthma Control Questionnaire (ACQ), ACQ-6 and ACQ-7

General

- All 6 or 7 items (5 most important symptoms, one question about [redacted] and one about [redacted] of ACQ have response on 0-6 ordinal scale ([redacted]). The total score is calculated as the average of all non-missing item responses [Asthma Control Questionnaire, Background, Administration and Analysis, April, 2008].
- ACQ-6 will be used at screening (visit 1). ACQ-7 will be used at all visit 2, 5, 7 or EW visit.

Questions, Responses and Calculation Method for ACQ

- Table below shows questions of ACQ.
- Each question has the response on 0-6 ordinal scale ([redacted]). The wordings of responses are not the same for all responses, but they are not described in this RAP.
- The total score for ACQ-7 is the mean of the response to the 7 questions. The total score for ACQ-6 is the mean of the response to the 6 questions excluding a question about [redacted]

Question	Item
	CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

Asthma Control Questionnaire (ACQ), ACQ-6 and ACQ-7

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

Handling of Missing Items

- Only one of the first five item responses are allowed to be missing in calculating the total scores for all versions of ACQ. One question about CCI (item 6) and one about CCI (item 7, for ACQ-7 only) are not allowed to be missing.
- If one of the first five item responses is missing, then total score will be calculated based on just the available data. This means missing value will be excluded from the denominator.

If there are unacceptable missing items, then ACQ will be regarded as missing.

Example

	Visit 2	Visit 5	Visit 7
Item 1	4	6	3
Item 2	3	5	4
Item 3	4	4	3
Item 4	5	5	4
Item 5	2	Missing	3
Item 6	4	4	2
Item 7	1	3	Missing

- ACQ-7 score at visit 2: (4 + 3 + 4 + 5 + 2 + 4 + 1) / 7 = 3.3

Since there is no missing value, ACQ-7 is calculated by using all 7 responses. Data will be rounded to one decimal place.

- ACQ-7 score at visit 5: (6 + 5 + 4 + 5 + 4 + 3) /6 = 4.5

Since there is one missing value for the first five item, ACQ-7 is calculated by using 6 responses.

- ACQ-7 score at visit 7: missing

Since question about CCI is missing, ACQ-7 should not be calculated and be missing at this visit.

St. George's Respiratory Questionnaire (SGRQ)

General

- Details for how to score the SGRQ, including handling of missing data, are outlined in the SGRQ manual (June, 2009).
- Changes from baseline in total score will be calculated.

Questions, Response and Weight for SGRQ

- Table below shows questions and responses of SGRQ, their weight for SGRQ score calculation and its number in aCRF.
- Each questionnaire response has a unique 'weight' to be used for score calculation.
- This questionnaire requests a single response to questions CCI, CCI and CCI. If multiple responses are given to one of these questions, then averaging the weights for the positive responses for that question are acceptable.
- SGRQ has three components: **Symptoms; Activity; Impacts**

SYMPTOMS COMPONENT

- This is calculated from the summed weights for the positive responses to questions CCI.

ACTIVITY COMPONENT

- This is calculated from the summed weights for the positive responses to questions CCI and CCI.

IMPACTS COMPONENT

- This is calculated from the summed weights for the positive responses to questions CCI, CCI and CCI.

TOTAL SCORE

- The Total score is calculated by summing all positive responses in the questionnaire and expressing the result as a percentage of the total weight for the questionnaire

Calculation method is described in next box.

Question	Item	Number in aCRF	Response	Weight
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.				

St. George's Respiratory Questionnaire (SGRQ)

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

St. George's Respiratory Questionnaire (SGRQ)

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

St. George's Respiratory Questionnaire (SGRQ)

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

St. George's Respiratory Questionnaire (SGRQ)

			CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

Calculation Method

Each component of the questionnaire is scored separately in three steps:

I. The weights for all items with positive responses are summed.
II. The weights for missed items are deducted from the maximum possible weight for each component. The weights for all missed items are deducted from the maximum possible weight for the Total score.
III. The score is calculated by dividing the summed weights by the adjusted maximum possible weight for that component and expressing the result as a percentage:

Score = CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

The Total score is calculated in similar way:

Score = CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

Sum of maximum possible weights for each component and Total:

- Symptoms: CCI
- Activity: CCI
- Impacts: CCI
- Total: CCI

Handling of Missing Items

Symptoms

The Symptoms component will tolerate **a maximum of 2 missed items**. The weight for the missed item is subtracted from the total possible weight for the Symptoms component (CCI) and from the Total weight (CCI).

Activity

The Activity component will tolerate **a maximum of 4 missed items.** The weight for the missed item is subtracted from the total possible weight for the Activity component (CCI) and from the Total weight (CCI).

St. George's Respiratory Questionnaire (SGRQ)

Impacts

The Impacts component will tolerate **a maximum of 6 missed items**. The weight for the missed item is subtracted from the total possible weight for the Impacts component ([redacted]) and from the Total weight ([redacted]).

If there were unacceptable number of missed items for any component, then SGRQ total score will be handled as missing.

Example

Table below is example data for calculation of SGRQ total score. Since this questionnaire requests a single response to questions [redacted], this table shows only one selected response for questions [redacted] (Data columns are [redacted]). For other questions, this table shows the results of [redacted]. In this example, it is assumed that there is no missed item.

In this study, each component score will not be calculated. However, we would like to show how to calculate each component score and total score in this example.

Symptoms

This is calculated from the summed weights for the positive responses to questions [redacted] In this example, weights for [redacted] data for questions [redacted] need to be summed. Summed weight is ([redacted]) = [redacted] Since maximum possible weight for symptoms is [redacted], symptoms component score can be calculated as [redacted]

Activity

This is calculated from the summed weights for the positive responses to questions [redacted] and [redacted]. In this example, weights for [redacted] data for questions [redacted] need to be summed. Summed weight is ([redacted]) = [redacted]. Since maximum possible weight for activity is [redacted], symptoms component score can be calculated as [redacted]

Impacts

This is calculated from the summed weights for the positive responses to questions [redacted] and [redacted]. In this example, weights for [redacted] data for questions [redacted] and weights for [redacted] data for questions [redacted] need to be summed. Summed weight is ([redacted]) = [redacted]. Since maximum possible weight for impacts is [redacted] symptoms component score can be calculated as [redacted]

Total

The Total score is calculated by summing all positive responses in the questionnaire and expressing the result as a percentage of the total weight for the questionnaire. Summed weights for total is summed weights for three components above, ([redacted]) = [redacted] Since maximum possible weight for total score is [redacted], SGRQ total score can be calculated as [redacted]

St. George's Respiratory Questionnaire (SGRQ)

Question	Item	Response	Weight	Data
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.				

St. George's Respiratory Questionnaire (SGRQ)

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded

St. George's Respiratory Questionnaire (SGRQ)

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded

Asthma Quality of Life Questionnaire (AQLQ)

General

- Details for how to score the AQLQ, including handling of missing data, are outlined in the AQLQ manual (June, 2005).
- Changes from baseline in total score will be calculated for the converted scores.

Questions, Responses and Calculation Method for AQLQ

- Table below shows questions of AQLQ.
- Each question has the response on a 7 – point scale ([redacted], [redacted], [redacted]). The wordings of responses are not the same for all responses, but they are not described in this RAP.
- Individual items are equally weighted. The overall AQLQ score is the mean of the responses to each of the 32 questions. Therefore, AQLQ score can be calculated to add all 32 responses together and divided the total by 32.
- AQLQ has four domains: Activity limitations, Symptoms, Emotional function, Environmental stimuli
  - Activity limitations: item: [redacted]
  - Symptoms: item: [redacted]
  - Emotional function: item: [redacted]
  - Environmental stimuli: item: [redacted]
- Note that only AQLQ total score will be calculated in this study, not each domain score. But acceptable missing items depends on each domain. Handling of missing items is described in next section

Question	Item
[redacted]	

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded

Handling of Missing Items

- Acceptable number of missed items
  - Activity limitations and Symptoms: **only one missing value per domain**
  - Emotional function, Environmental stimuli: **Not accept any missing responses**

- If there are missing items, then total score will be calculated based on just the available data.

This means missing value will be excluded from the denominator.

- If there were unacceptable number of missed items for any component, then AQLQ total score will be handled as missing.

Example

	Visit 2	Visit 5	Visit 7
Item 1	3	missing	5
Item 2	4	1	6
Item 3	3	2	5
Item 4	4	2	3
Item 5	2	2	4
Item 6	1	missing	5
Item 7	4	1	missing
Item 8	6	4	7
Item 9	4	2	6
Item 10	3	3	5
Item 11	4	5	4
Item 12	5	2	3
Item 13	4	4	2
Item 14	2	2	1
Item 15	3	3	2
Item 16	4	4	3
Item 17	5	5	4
Item 18	6	2	5
Item 19	2	3	6
Item 20	4	4	7
Item 21	5	5	4
Item 22	6	7	4
Item 23	3	4	4
Item 24	2	2	5
Item 25	4	4	6
Item 26	5	5	7
Item 27	6	6	3
Item 28	2	6	4
Item 29	4	2	5
Item 30	5	5	6
Item 31	6	5	2
Item 32	4	5	3

- AQLQ total score at visit 2: (3 + 4 + 3 + , , , + 5 + 6 + 4) / 32 = 3.9

Since there is no missing value, AQLQ total score is calculated by using all 32 responses. Data will

be rounded to one decimal place.

- AQLQ total score at visit 5: (1 + 2 + 2 + , , , + 5 + 5 + 5) /30 = 3.6

Although there is one missing value for Activity limitations domain (item 1) and one for Symptoms domain (item 6), the number of missed items is acceptable. AQLQ total score is calculated by using 30 responses available.

- AQLQ total score at visit 7: missing

Since one response for Emotional function domain (item 7) is missing and this is not acceptable, AQLQ total score should not be calculated and be missing at this visit.

11.7. Appendix 7: Reporting Standards for Missing Data

11.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion (i.e. as specified in the protocol) was defined as he/she has completed all phases of the study including the safety follow-up telephone contact or clinic visit. • 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 not be slotted and not be summarized as Withdrawal visit.

11.7.2. Handling of Missing Data

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

11.7.2.1. 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 does not allow 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. • 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/ Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month o If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

11.8. Appendix 8: Values of Potential Clinical Importance

This is not applicable to this study.

11.9. Appendix 9: Implementation and mitigation strategy of Statistical Output Review (SOR)

This appendix describes what Japan S&P team will do as SOR and its mitigation strategy to maintain integrity of study.

Background:

In this study, SOR will be planned before release of randomization code from RandAll. The purpose of SOR is to make sure programming was in place and to check formatting of outputs, NOT to review the data itself. According to GSK SOP_57860, a dry run on a single arm open label study is the same as an interim analysis, so unless it's detailed in the protocol, that should not be done. Therefore, the mitigation strategy should be described in this RAP.

What Japan S&P team will do:

- Lead statistician and lead programmer will make sure programming was in place and to check formatting of outputs.
- Additional reviewers in Japan S&P will help to make sure programming works well and check formatting of outputs.

Mitigation strategy:

- Japan S&P team will NOT share any results with outside of Japan S&P team at the timing of SOR or prior to interim SAC.
- HARP environment will also be restricted to Japan S&P team and programmers.

11.10. Appendix 10: Abbreviations & Trade Marks

11.10.1. 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
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
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
MACE	Major Adverse Cardiac Event
MMRM	Mixed Model Repeated Measures
PCI	Potential Clinical Importance
PDMP	Protocol Deviation Management Plan
PLS	Plain Language Summary
PP	Per Protocol
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
SAC	Statistical Analysis Complete
SDSP	Study Data Standardization Plan
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure

Abbreviation	Description
TA	Therapeutic Area
TFL	Tables, Figures & Listings

11.10.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
ELLIPTA

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS

11.11. Appendix 11: List of Data Displays

11.11.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

At interim analysis:

Section	Tables	Figures
Study Population	1.1 to 1.n	NA
Safety	2.1 to 2.n	NA
Other	3.1 to 3.n	NA
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	y to z	

At final analysis:

Section	Tables	Figures
Study Population	11.1 to 1.n	NA
Safety	12.1 to 2.n	NA
Other	13.1 to 3.n	NA
Section	**Listings**	
ICH Listings	44 to x	
Other Listings	y to z	

11.11.2. Deliverables

Delivery [Priority] [1]	Description
IA [X]	Interim Analysis Statistical Analysis Complete
SAC [X]	Final Statistical Analysis Complete

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

11.11.3. Study Population Tables (interim)

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	ITT	ES1	Summary of Subject Disposition (Interim)	ICH E3, FDAAA, EudraCT	IA [1]
1.2.	ITT	SD1	Summary of Treatment Status (Interim)	ICH E3	IA [1]
1.3.	Enrolled	ES4	Summary of Participant Disposition at Each Study Epoch (Interim)	ICH E3	IA [1]
1.4.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure and Run-in Failure (Interim)	Journal Requirements	IA [1]
1.5.	Enrolled	NS1	Summary of Number of Participant by Country and Site ID (Interim)	EudraCT/Clinical Operations	IA [1]
Protocol Deviation					
1.6.	ITT	DV1	Summary of Important Protocol Deviations (Interim)	ICH E3	IA [1]
Population Analysed					
1.7.	All Subjects	SP1	Summary of Study Populations (Interim)	IDSL	IA [1]
Demographic and Baseline Characteristics					
1.8.	ITT	DM1	Summary of Demographic Characteristics (Interim)	ICH E3, FDAAA, EudraCT	IA [1]
1.9.	Enrolled	DM11	Summary of Age Ranges (Interim)	EudraCT	IA [1]
1.10.	ITT	DM5	Summary of Race and Racial Combinations (Interim)	ICH E3, FDA, FDAAA, EudraCT	IA [1]
1.11.	ITT	Study Specific	Summary of Disease Duration (Interim)		IA [1]
1.12.	ITT	Study Specific	Summary of Asthma Medical History Questionnaire (Interim)		IA [1]
1.13.	ITT	Study Specific	Summary of Exacerbation History (Interim)		IA [1]
1.14.	ITT	SU1 (subset)	Summary of Smoking Status (Interim)		IA [1]

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.15.	ITT	Study Specific	Summary of Cardiovascular History / Risk Factors (Interim)		IA [1]
1.16.	ITT	FH1	Summary of Family History of Cardiovascular Risk Factors (Interim)		IA [1]
1.17.	ITT	Study Specific	Summary of ACQ-6 score at Screening (Interim)		IA [1]
1.18.	ITT	Study Specific	Summary of Clinic Spirometry at Baseline (Interim)		IA [1]
Prior and Concomitant Medications					
1.19.	ITT	MH4	Summary of Current Medical Conditions (Interim)	ICH E3	IA [1]
1.20.	ITT	MH4	Summary of Past Medical Conditions (Interim)	ICH E3	IA [1]
1.21.	ITT	CM1	Summary of Asthma Concomitant Medications Before Study Treatment (Interim)		IA [1]
1.22.	ITT	CM1	Summary of Asthma Concomitant Medications During the Treatment Period (Interim)		IA [1]
1.23.	ITT	CM1	Summary of Non-Asthma Concomitant Medications During the Treatment Period (Interim)		IA [1]
Exposure and Treatment Compliance					
1.24.	ITT	Study Specific	Summary of Treatment Compliance (Interim)		IA [1]

11.11.4. Study Population Tables (final)

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
11.1.	ITT	ES1	Summary of Subject Disposition	ICH E3, FDAAA, EudraCT	SAC [1]
11.2.	ITT	SD1	Summary of Treatment Status	ICH E3	SAC [1]
11.3.	Enrolled	ES4	Summary of Participant Disposition at Each Study Epoch	ICH E3	SAC [1]
Protocol Deviation					
11.4.	ITT	DV1	Summary of Important Protocol Deviations	ICH E3	SAC [1]
Population Analysed					
11.5.	All Subjects	SP1	Summary of Study Populations	IDSL	SAC [1]
Demographic and Baseline Characteristics					
11.6.	ITT	DM1	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	SAC [1]
11.7.	Enrolled	DM11	Summary of Age Ranges	EudraCT	SAC [1]
11.8.	ITT	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT	SAC [1]
11.9.	ITT	Study Specific	Summary of Disease Duration		SAC [1]
11.10.	ITT	Study Specific	Summary of Asthma Medical History Questionnaire		SAC [1]
11.11.	ITT	Study Specific	Summary of Exacerbation History		SAC [1]
11.12.	ITT	SU1 (subset)	Summary of Smoking Status		SAC [1]
11.13.	ITT	Study Specific	Summary of Cardiovascular History / Risk Factors		SAC [1]
11.14.	ITT	FH1	Summary of Family History of Cardiovascular Risk Factors		SAC [1]
11.15.	ITT	Study Specific	Summary of ACQ-6 score at Screening		SAC [1]
11.16.	ITT	Study Specific	Summary of Clinic Spirometry at Baseline		IA [1]

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Prior and Concomitant Medications					
11.17.	ITT	MH4	Summary of Current Medical Conditions	ICH E3	SAC [1]
11.18.	ITT	CM1	Summary of Asthma Concomitant Medications During the Treatment Period		SAC [1]
11.19.	ITT	CM1	Summary of Asthma Concomitant Medications During the Follow-Up Period		SAC [1]
11.20.	ITT	CM1	Summary of Non-Asthma Concomitant Medications During the Treatment Period		SAC [1]
11.21.	ITT	CM1	Summary of Non-Asthma Concomitant Medications During the Follow-Up Period		SAC [1]
Exposure and Treatment Compliance					
11.22.	ITT	Study Specific	Summary of Treatment Compliance		SAC [1]

11.11.5. Safety Tables (interim)

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Treatment Exposure					
2.1.	ITT	EX1	Summary of Exposure to Study Treatment (Interim)	ICH E3	IA [1]
Adverse Events (AEs)					
2.2.	ITT	AE13	Summary of All Adverse Events Overview During Treatment Period (Interim)	ICH E3	IA [1]
2.3.	ITT	AE1	Summary of All Adverse Events During Treatment Period (Interim)	ICH E3	IA [1]
2.4.	ITT	Study Specific	Summary of All Adverse Events During Treatment Period per Thousand Person-Year (Interim)		
2.5.	ITT	AE5A	Summary of All Adverse Events During Treatment Period by maximum severity (Interim)	ICH E3	IA [1]
2.6.	ITT	AE1	Summary of All Drug-Related Adverse Events During Treatment Period (Interim)	ICH E3	IA [1]
2.7.	ITT	Study Specific	Summary of All Drug-Related Adverse Events During Treatment Period per Thousand Person-Year (Interim)		IA [1]
2.8.	ITT	AE3	Summary of Most Common Adverse Events (3% or more of Subjects in Any Treatment Group) During Treatment Period by dose group (interim)	ICH E3 3% or more of Subjects in Any Treatment Group	IA [1]
2.9.	ITT	Study Specific	Summary of Adverse Events for week 0-12 and week 13-24 During Treatment Period (interim)		IA [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.10.	ITT	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term During Treatment Period (Number of Participant and Occurrences) (Interim)	FDAAA, EudraCT 'Common' to be defined by study/project team. For studies with very few events/participants, listing is sufficient: discuss this option with your disclosure representative.	IA [1]
Serious and Other Significant Adverse Events					
2.11.	ITT	AE1	Summary of Serious Adverse Events During Treatment Period (Interim)		IA [1]
2.12.	ITT	Study Specific	Summary of Serious Adverse Events During Treatment Period per Thousand Person-Year (Interim)		IA [1]
2.13.	ITT	AE1	Summary of Adverse Events Leading to Withdrawal from Study During Treatment Period (Interim)		IA [1]
2.14.	ITT	AE1	Summary of Adverse Events of Special Interest During Treatment Period (Interim)		IA [1]
2.15.	ITT	Study Specific	Summary of Adverse Events of Special Interest During Treatment Period per Thousand Person-Year (Interim)		IA [1]
2.16.	ITT	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term during treatment period (Number of Participants and Occurrences) (Interim)	FDAAA, EudraCT For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative.	IA [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
MACE					
2.17.	ITT	Study Specific	Summary of Major Cardiac Events (MACE) – Narrow Definition (Interim)		IA [1]
2.18.	ITT	Study Specific	Summary of Major Cardiac Events (MACE) – Broad Definition (Interim)		IA [1]
Laboratory: Chemistry					
2.19.	ITT	LB1	Summary of Chemistry Data (Interim)		IA [1]
2.20.	ITT	LB1	Summary of Chemistry Changes from Baseline (Interim)	ICH E3 Includes Baseline values. Includes pre-specified parameters repeated in conventional units.	IA [1]
2.21.	ITT	LB3	Summary of Chemistry Shifts from Baseline Relative to Normal Range (Interim)		IA [1]
Laboratory: Hematology					
2.22.	ITT	LB1	Summary of Hematology Data (Interim)		IA [1]
2.23.	ITT	LB1	Summary of Hematology Changes from Baseline (Interim)	ICH E3 Includes baseline values.	IA [1]
2.24.	ITT	LB3	Summary of Hematology Shifts from Baseline Relative to Normal Range (Interim)		IA [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Urinalysis					
2.25.	ITT	UR1	Summary of Worst Case Urinalysis Results (Discrete or Character Values) Post-Baseline Relative to Baseline (Interim)	ICH E3 As above for Chemistry, using dipstick categories. Define change categories according to actual values expected from lab dataset	IA [1]
Vital Signs					
2.26.	ITT	VS1	Summary of Vital Signs (Interim)	ICH E3 Includes Baseline values.	IA [1]
2.27.	ITT	VS1	Summary of Change from Baseline in Vital Signs (Interim)	ICH E3 Includes Baseline values.	IA [1]
ECG					
2.28.	ITT	EG2	Summary of ECG Values (Interim)	IDSL	IA [1]
2.29.	ITT	EG2	Summary of Change from Baseline in ECG Values (Interim)	IDSL	IA [1]
2.30.	ITT	Study Specific	Summary of Categories for QTc (F) Values (Interim)	IDSL	IA [1]
2.31.	ITT	Study Specific	Summary of Categories for Change from Baseline in QTc (F) Values (Interim)	IDSL	IA [1]
2.32.	ITT	EG1	Summary of ECG Findings (Interim)	IDSL As above for Chemistry, using ECG findings categories (and change from baseline categories, if applicable).	IA [1]
2.33.	ITT	Study Specific	Summary of ECG Findings Shifts from Baseline (Interim)		IA [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pneumonia and Radiography (Chest X-Rays)					
2.34.	ITT	Study Specific	Summary of On-Treatment Pneumonia, Including Chest X-ray Finding (Interim)	IDSL	IA [1]

11.11.6. Safety Tables (final)

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Treatment Exposure					
12.1.	ITT	EX1	Summary of Exposure to Study Treatment	ICH E3	SAC [1]
Adverse Events (AEs)					
12.2.	ITT	AE13	Summary of All Adverse Events Overview During Treatment Period	ICH E3	SAC [1]
12.3.	ITT	AE1	Summary of All Adverse Events During Treatment Period by dose group	ICH E3	SAC [1]
12.4.	ITT	AE1	Summary of All Adverse Events During Treatment Period by dose at AE (dose: FF/UMEC/VI 100/62.5/25)	ICH E3	SAC [1]
12.5.	ITT	AE1	Summary of All Adverse Events During Treatment Period by dose at AE (dose: FF/UMEC/VI 200/62.5/25)	ICH E3	SAC [1]
12.6.	ITT	AE1	Summary of All Adverse Events During Follow-Up Period by dose group	ICH E3	SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
12.7.	ITT	Study Specific	Summary of All Adverse Events During Treatment Period per Thousand Person-Year by dose group		
12.8.	ITT	AE5A	Summary of All Adverse Events During Treatment Period by maximum severity and dose group	ICH E3	SAC [1]
12.9.	ITT	AE5A	Summary of All Adverse Events During Treatment Period by maximum severity and dose at AE (dose: FF/UMEC/VI 100/62.5/25)	ICH E3	SAC [1]
12.10.	ITT	AE5A	Summary of All Adverse Events During Treatment Period by maximum severity and dose at AE (dose: FF/UMEC/VI 200/62.5/25)	ICH E3	SAC [1]
12.11.	ITT	AE1	Summary of All Drug-Related Adverse Events During Treatment Period by dose group	ICH E3	SAC [1]
12.12.	ITT	AE1	Summary of All Drug-Related Adverse Events During Treatment Period by dose at AE (dose: FF/UMEC/VI 100/62.5/25)	ICH E3	SAC [1]
12.13.	ITT	AE1	Summary of All Drug-Related Adverse Events During Treatment Period by dose at AE (dose: FF/UMEC/VI 200/62.5/25)	ICH E3	SAC [1]
12.14.	ITT	Study Specific	Summary of All Drug-Related Adverse Events During Treatment Period per Thousand Person-Year by dose group		SAC [1]
12.15.	ITT	AE3	Summary of Most Common Adverse Events (3% or more of Subjects in Any Treatment Group) During Treatment Period by dose group	ICH E3	SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
12.16.	ITT	AE3	Summary of Most Common Adverse Events (3% or more of Subjects in Any Treatment Group) During Treatment Period by dose at AE (dose: FF/UMEC/VI 100/62.5/25)	ICH E3	SAC [1]
12.17.	ITT	AE3	Summary of Most Common Adverse Events (3% or more of Subjects in Any Treatment Group) During Treatment Period by dose at AE (dose: FF/UMEC/VI 200/62.5/25)	ICH E3	SAC [1]
12.18.	ITT	Study Specific	Summary of Adverse Events for week 0-12, week 13-24, week 25-36 and week 37-52 During Treatment Period by dose group		SAC [1]
12.19.	ITT	Study Specific	Summary of Adverse Events for week 0-24, week 25-52 During Treatment Period by dose group		SAC [1]
12.20.	ITT	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term During Treatment Period (Number of Participant and Occurrences)	FDAAA, EudraCT 'Common' to be defined by study/project team. For studies with very few events/participants, listing is sufficient: discuss this option with your disclosure representative.	SAC [1]
12.21.	ITT	AE3	Summary of Non-Serious Drug-Related Adverse Events During Treatment Period by dose group	PLS	SAC [1]
12.22.	ITT	AE1	Summary of All Drug-Related Adverse Events During Treatment Period and Follow-Up Period by dose group		SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Serious and Other Significant Adverse Events					
12.23.	ITT	AE1	Summary of Serious Adverse Events During Treatment Period by dose group		SAC [1]
12.24.	ITT	AE1	Summary of Serious Adverse Events During Treatment Period by dose at AE (dose: FF/UMEC/VI 100/62.5/25)		SAC [1]
12.25.	ITT	AE1	Summary of Serious Adverse Events During Treatment Period by dose at AE (dose: FF/UMEC/VI 200/62.5/25)		SAC [1]
12.26.	ITT	Study Specific	Summary of Serious Adverse Events During Treatment Period per Thousand Person-Year by dose group		IA [1]
12.27.	ITT	AE1	Summary of Adverse Events Leading to Withdrawal from Study During Treatment Period by dose group		SAC [1]
12.28.	ITT	AE1	Summary of Adverse Events Leading to Withdrawal from Study During Treatment Period by dose at AE (dose: FF/UMEC/VI 100/62.5/25)		SAC [1]
12.29.	ITT	AE1	Summary of Adverse Events Leading to Withdrawal from Study During Treatment Period by dose at AE (dose: FF/UMEC/VI 200/62.5/25)		SAC [1]
12.30.	ITT	AE1	Summary of Adverse Events of Special Interest During Treatment Period by dose group		SAC [1]
12.31.	ITT	AE1	Summary of Adverse Events of Special Interest During Treatment Period by dose at AE (dose: FF/UMEC/VI 100/62.5/25)		SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
12.32.	ITT	AE1	Summary of Adverse Events of Special Interest During Treatment Period by dose at AE (dose: FF/UMEC/VI 200/62.5/25)		SAC [1]
12.33.	ITT	Study Specific	Summary of Adverse Events of Special Interest During Treatment Period per Thousand Person-Year by dose group		IA [1]
12.34.	ITT	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term during treatment period (Number of Participants and Occurrences)	FDAAA, EudraCT For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative.	SAC [1]
12.35.	ITT	AE3	Summary of Serious Drug-Related Adverse Events by dose group	PLS	SAC [1]
MACE					
12.36.	ITT	Study Specific	Summary of Major Cardiac Events (MACE) – Narrow Definition		SAC [1]
12.37.	ITT	Study Specific	Summary of Major Cardiac Events (MACE) – Broad Definition		SAC [1]
Laboratory: Chemistry					
12.38.	ITT	LB1	Summary of Chemistry Data		SAC [1]
12.39.	ITT	LB1	Summary of Chemistry Changes from Baseline	ICH E3 Includes Baseline values. Includes pre-specified parameters repeated in conventional units.	SAC [1]
12.40.	ITT	LB3	Summary of Chemistry Shifts from Baseline Relative to Normal Range		SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Hematology					
12.41.	ITT	LB1	Summary of Hematology Data		SAC [1]
12.42.	ITT	LB1	Summary of Hematology Changes from Baseline	ICH E3 Includes baseline values.	SAC [1]
12.43.	ITT	LB3	Summary of Hematology Shifts from Baseline Relative to Normal Range		SAC [1]
Laboratory: Urinalysis					
12.44.	ITT	UR1	Summary of Worst Case Urinalysis Results (Discrete or Character Values) Post-Baseline Relative to Baseline	ICH E3 As above for Chemistry, using dipstick categories. Define change categories according to actual values expected from lab dataset	SAC [1]
Vital Signs					
12.45.	ITT	VS1	Summary of Vital Signs	ICH E3 Includes Baseline values.	SAC [1]
12.46.	ITT	VS1	Summary of Change from Baseline in Vital Signs	ICH E3 Includes Baseline values.	SAC [1]
ECG					
12.47.	ITT	EG2	Summary of ECG Values	IDSL	SAC [1]
12.48.	ITT	EG2	Summary of Change from Baseline in ECG Values	IDSL	SAC [1]
12.49.	ITT	Study Specific	Summary of Categories for QTc (F) Values (Interim)	IDSL	SAC [1]
12.50.	ITT	Study Specific	Summary of Categories for Change from Baseline in QTc (F) Values (Interim)	IDSL	SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
12.51.	ITT	EG1	Summary of ECG Findings	IDSL As above for Chemistry, using ECG findings categories (and change from baseline categories, if applicable).	SAC [1]
12.52.	ITT	Study Specific	Summary of ECG Findings Shifts from Baseline		SAC [1]
Pneumonia and Radiography (Chest X-Rays)					
12.53.	ITT	Study Specific	Summary of On-Treatment Pneumonia, Including Chest X-ray Finding	IDSL	SAC [1]

11.11.7. Other Tables (interim)

Other Endpoint: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Other Endpoints					
3.1.	ITT	Study Specific	Summary of Trough FEV_1 (L) (Interim)		IA [1]
3.2.	ITT	Study Specific	Summary of ACQ-7 Total Score (Interim)		IA [1]
3.3.	ITT	Study Specific	Summary of SGRQ Total Score (Interim)		IA [1]
3.4.	ITT	Study Specific	Summary of AQLQ Total Score (Interim)		IA [1]
3.5.	ITT	Study Specific	Summary of Severe Asthma Exacerbations (Interim)		IA [1]
3.6.	ITT	Study Specific	Summary of Moderate/Severe Asthma Exacerbations (Interim)		IA [1]

11.11.8. Other Tables (final)

Other Endpoint: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Other Endpoints					
13.1.	ITT	Study Specific	Summary of Trough FEV_1 (L)		SAC [1]
13.2.	ITT	Study Specific	Summary of ACQ-7 Total Score		SAC [1]
13.3.	ITT	Study Specific	Summary of SGRQ Total Score		SAC [1]
13.4.	ITT	Study Specific	Summary of AQLQ Total Score		SAC [1]
13.5.	ITT	Study Specific	Summary of Unscheduled Asthma-Related Healthcare Resource Utilization Over the 52 Weeks of the Treatment Period		SAC [1]
13.6.	ITT	Study Specific	Summary of Severe Asthma Exacerbations		SAC [1]
13.7.	ITT	Study Specific	Summary of Moderate/Severe Asthma Exacerbations		SAC [1]
13.8.	ITT	Study Specific	Summary of Annualized rate of Severe Asthma Exacerbations and Moderate/Severe Asthma Exacerbations		SAC [1]

11.11.9. ICH Listings (interim)

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Screened	ES7	Listing of Reasons for Screen Failure or Run-in Failure	Journal Guidelines	IA [1]
2.	ITT	ES2	Listing of Reasons for Study Withdrawal	ICH E3 Required for all studies except single dose studies.	IA [1]
3.	ITT	SD3	Listing of Reasons for Study Treatment Discontinuation	ICH E3	IA [1]
4.	ITT	TA1	Listing of Planned and Actual Treatments	IDSL Note: IDSL shell in development.	IA [1]
Protocol Deviations					
5.	ITT	DV2	Listing of Important Protocol Deviations	ICH E3 Listing also includes analysis population exclusions.	IA [1]
6.	ITT	IE3	Listing of Participants with Inclusion/Exclusion Criteria Deviations	ICH E3	IA [1]
Populations Analysed					
7.	Enrolled	SP3	Listing of Participants Excluded from Any Population	ICH E3 e.g., participants screened but not randomized, participants randomized but not treated, participants with deviations leading to exclusion from per protocol population (can be separate listing per population).	IA [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Demographic and Baseline Characteristics					
8.	ITT	DM2	Listing of Demographic Characteristics	ICH E3	IA [1]
9.	ITT	DM9	Listing of Race	ICH E3	IA [1]
Prior and Concomitant Medications					
10.	ITT	CM3	Listing of Asthma Concomitant Medications		IA [1]
11.	ITT	CM3	Listing of Non-Asthma Concomitant Medications		IA [1]
12.	ITT	CM6	Relationship between ATC Level 1, Ingredient and Verbatim Text for Non-Asthma Medications		IA [1]
Exposure and Treatment Compliance					
13.	ITT	EX3	Listing of Exposure Data	ICH E3	IA [1]
14.	ITT	Study Specific	Listing of Treatment Compliance Data	ICH E3	IA [1]
Adverse Events					
15.	ITT	AE8	Listing of All Adverse Events	ICH E3	IA [1]
16.	ITT	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	IA [1]
17.	ITT	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	IA [1]
Serious and Other Significant Adverse Events					
18.	ITT	AE8	Listing of Fatal Serious Adverse Events	ICH E3 Fatal and Non-Fatal SAEs are combined into a single listing for ClinPharm studies (i.e., “Listing of Serious Adverse Events”).	IA [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
19.	ITT	AE8	Listing of Non-Fatal Serious Adverse Events	ICH E3 Fatal and Non-Fatal SAEs are combined into a single listing for ClinPharm studies (i.e., "Listing of Serious Adverse Events").	IA [1]
20.	ITT	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	IA [1]
21.	ITT	AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	IA [1]
22.	ITT	AE8	Listing of Adverse Events of Special Interest	ICH E3 Required for studies where interventions other than withdrawal from treatment or study are possible.	IA [1]
Hepatobiliary (Liver)					
23.	ITT	MH2	Listing of Medical Conditions for Participants with Liver Stopping Events	IDSL	IA [1]
24.	ITT	SU2	Listing of Substance Use for Participants with Liver Stopping Events	IDSL	IA [1]
25.	ITT	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting	IDSL	IA [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
All Laboratory					
26.	ITT	LB5	Listing of Chemistry Values for Subjects with Any Value Outside Normal Range	ICH E3 May be split into separate listings by chemistry, hematology, etc. Display ALL labs for a subject who experienced a value of potential clinical importance.	IA [1]
27.	ITT	LB5	Listing of Haematology Values for Subjects with Any Value Outside Normal Range	ICH E3 May be split into separate listings by chemistry, hematology, etc. Display ALL labs for a subject who experienced a value of potential clinical importance.	IA [1]
ECG					
28.	ITT	EG3 (modified)	Listing of ECG Values for Subjects with any Abnormal ECG Finding	IDSL Required for ClinPharm studies only.	IA [1]
29.	ITT	EG5	Listing of Abnormal ECG Findings	IDSL Required for ClinPharm studies only.	IA [1]
Vital Signs					
30.	ITT	VS4	Listing of Vital Signs	IDSL Required for ClinPharm studies only.	IA [1]

11.11.10. Non-ICH Listings (interim)

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population					
31.	ITT	MH2	Listing of Medical Conditions		IA [1]
32.	ITT	Study Specific	Listing of Family History of Cardiovascular Risk Factors		IA [1]
33.	ITT	Study Specific	Listing of Asthma Duration and Exacerbation History		IA [1]
34.	ITT	SU2	Listing of Smoking History and Status		IA [1]
35.	ITT	Study Specific	Listing of Inhaler Malfunctions		IA [1]
36.	ITT	Study Specific	Listing of Clinic Spirometry at Baseline		IA [1]
Other					
37.	ITT	Study Specific	Listing of Trough FEV1 (L) Data		IA [1]
38.	ITT	Study Specific	Listing of ACQ Scores		IA [1]
39.	ITT	Study Specific	Listing of SGRQ Scores		IA [1]
40.	ITT	Study Specific	Listing of AQLQ Scores		IA [1]
41.	ITT	Study Specific	Listing of Moderate/Severe Asthma Exacerbations		IA [1]
Safety					
42.	ITT	Study Specific	Listing of Pneumonia Data, including Chest X-ray Finding		IA [1]
43.	ITT	Study Specific	Listing of Bone Fracture Data		IA [1]

11.11.11. ICH Listings (final)

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
44.	Screened	ES7	Listing of Reasons for Screen Failure or Run-in Failure	Journal Guidelines	SAC [1]
45.	ITT	ES2	Listing of Reasons for Study Withdrawal	ICH E3 Required for all studies except single dose studies.	SAC [1]
46.	ITT	SD3	Listing of Reasons for Study Treatment Discontinuation	ICH E3	SAC [1]
47.	ITT	TA1	Listing of Planned and Actual Treatments	IDSL Note: IDSL shell in development.	SAC [1]
Protocol Deviations					
48.	ITT	DV2	Listing of Important Protocol Deviations	ICH E3 Listing also includes analysis population exclusions.	SAC [1]
49.	ITT	IE3	Listing of Participants with Inclusion/Exclusion Criteria Deviations	ICH E3	SAC [1]
Populations Analysed					
50.	Enrolled	SP3	Listing of Participants Excluded from Any Population	ICH E3 e.g., participants screened but not randomized, participants randomized but not treated, participants with deviations leading to exclusion from per protocol population (can be separate listing per population).	SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Demographic and Baseline Characteristics					
51.	ITT	DM2	Listing of Demographic Characteristics	ICH E3	SAC [1]
52.	ITT	DM9	Listing of Race	ICH E3	SAC [1]
Prior and Concomitant Medications					
53.	ITT	CM3	Listing of Asthma Concomitant Medications		SAC [1]
54.	ITT	CM3	Listing of Non-Asthma Concomitant Medications		SAC [1]
55.	ITT	CM6	Relationship between ATC Level 1, Ingredient and Verbatim Text for Non-Asthma Medications		SAC [1]
Exposure and Treatment Compliance					
56.	ITT	EX3	Listing of Exposure Data	ICH E3	SAC [1]
57.	ITT	Study Specific	Listing of Treatment Compliance Data	ICH E3	SAC [1]
Adverse Events					
58.	ITT	AE8	Listing of All Adverse Events	ICH E3	SAC [1]
59.	ITT	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	SAC [1]
60.	ITT	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	SAC [1]
Serious and Other Significant Adverse Events					
61.	ITT	AE8	Listing of Fatal Serious Adverse Events	ICH E3 Fatal and Non-Fatal SAEs are combined into a single listing for ClinPharm studies (i.e., “Listing of Serious Adverse Events”).	SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
62.	ITT	AE8	Listing of Non-Fatal Serious Adverse Events	ICH E3 Fatal and Non-Fatal SAEs are combined into a single listing for ClinPharm studies (i.e., "Listing of Serious Adverse Events").	SAC [1]
63.	ITT	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	SAC [1]
64.	ITT	AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	SAC [1]
65.	ITT	AE8	Listing of Adverse Events of Special Interest	ICH E3 Required for studies where interventions other than withdrawal from treatment or study are possible.	SAC [1]
Hepatobiliary (Liver)					
66.	ITT	MH2	Listing of Medical Conditions for Participants with Liver Stopping Events	IDSL	SAC [1]
67.	ITT	SU2	Listing of Substance Use for Participants with Liver Stopping Events	IDSL	SAC [1]
68.	ITT	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting	IDSL	SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
All Laboratory					
69.	ITT	LB5	Listing of Chemistry Values for Subjects with Any Value Outside Normal Range	ICH E3 May be split into separate listings by chemistry, hematology, etc. Display ALL labs for a subject who experienced a value of potential clinical importance.	SAC [1]
70.	ITT	LB5	Listing of Haematology Values for Subjects with Any Value Outside Normal Range	ICH E3 May be split into separate listings by chemistry, hematology, etc. Display ALL labs for a subject who experienced a value of potential clinical importance.	SAC [1]
71.	ITT	UR2A	Listing of Urinalysis Data (Protein and Occult Blood)	Protein and occult blood only. All subjects data need to be displayed.	SAC [1]
ECG					
72.	ITT	EG3 (modified)	Listing of ECG Values for Subjects with any Abnormal ECG Finding	IDSL Required for ClinPharm studies only.	SAC [1]
73.	ITT	EG5	Listing of Abnormal ECG Findings	IDSL Required for ClinPharm studies only.	SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Vital Signs					
74.	ITT	VS4	Listing of Vital Signs	IDSL Required for ClinPharm studies only.	SAC [1]

11.11.12. Non-ICH Listings (final)

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population					
75.	ITT	MH2	Listing of Medical Conditions		SAC [1]
76.	ITT	Study Specific	Listing of Family History of Cardiovascular Risk Factors		SAC [1]
77.	ITT	Study Specific	Listing of Asthma Duration and Exacerbation History		SAC [1]
78.	ITT	SU2	Listing of Smoking History and Status		SAC [1]
79.	ITT	Study Specific	Listing of Inhaler Malfunctions		SAC [1]
80.	ITT	Study Specific	Listing of Clinic Spirometry at Baseline		SAC [1]
Other					
81.	ITT	Study Specific	Listing of Trough FEV1 (L) Data		SAC [1]
82.	ITT	Study Specific	Listing of ACQ Scores		SAC [1]
83.	ITT	Study Specific	Listing of SGRQ Scores		SAC [1]
84.	ITT	Study Specific	Listing of AQLQ Scores		SAC [1]

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
85.	ITT	Study Specific	Listing of Unscheduled Asthma-Related Healthcare Resource Utilization Over the 52		SAC [1]
86.	ITT	Study Specific	Listing of Moderate/Severe Asthma Exacerbations		SAC [1]
Safety					
87.	ITT	Study Specific	Listing of Pneumonia Data, including Chest X-ray Finding		SAC [1]
88.	ITT	Study Specific	Listing of Bone Fracture Data		SAC [1]
89.	ITT	LIVER5	Listing of Liver Event Results and Time of Event Relative to Treatment		SAC [1]
90.	ITT	LIVER6	Listing of Liver Event Information for RUCAM Score		SAC [1]
91.	ITT	LIVER7	Listing of Liver Biopsy Details		SAC [1]
92.	ITT	LIVER8	Listing of Liver Imaging Details		SAC [1]
93.	Screened	IDSL	Patient Profile for Arrhythmias		SAC [1]
94.	Screened	IDSL	Patient Profile for Congestive Heart Failure		SAC [1]
95.	Screened	IDSL	Patient Profile for Cerebrovascular Events/Stroke		SAC [1]
96.	Screened	IDSL	Patient Profile for Deep Vein Thrombosis / Pulmonary Embolism		SAC [1]
97.	Screened	IDSL	Patient Profile for Myocardial Infarction / Unstable Angina		SAC [1]
98.	Screened	IDSL	Patient Profile for Hypertension		SAC [1]
99.	Screened	IDSL	Patient Profile for Revascularization		SAC [1]
100.	Screened	IDSL	Patient Profile for Valvulopathy		SAC [1]
101.	Screened	IDSL	Patient Profile for All Cause Deaths		SAC [1]