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

Effective Date: Should correspond with the date of last RAP approval. For example, if the final Lead Author and Programmer Line Managers / Designees approved on different days, the date the last person approved is documented as the effective date.

Title	:	Reporting and Analysis Plan for Study 207626: A Phase IV, 12 week, randomised, double-blind, double-dummy study to compare single inhaler triple therapy, fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI), with tiotropium monotherapy based on lung function and symptoms in participants with chronic obstructive pulmonary disease
Compound Number	:	GSK2834425 (GW685698 + GSK573719 + GW642444)
Effective Date	:	30-JUL-2019

Description:

The purpose of this reporting and analysis plan (RAP) is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 207626.

This document will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable and will serve as a detailed guide for the programming team.

RAP Author(s):

Author	Date
PPD Associate Director, Biostatistics, PAREXEL International	24-Jul-2019

RAP Team Review Confirmations
(Method: E-mail)

Reviewer	Date
PPD Lead Study Statistician, Principal Statistician (Respiratory Clinical Statistics)	25-Jul-2019
PPD Programming Manager (Respiratory Clinical Programming)	25-Jul-2019
PPD Medical Director (Safety Evaluation and Risk Management, Global Clinical Safety and Pharmacovigilance)	25-Jul-2019
PPD Medical Director (Safety Evaluation and Risk Management, Global Clinical Safety and Pharmacovigilance)	24-Jul-2019
PPD Director (Respiratory, Clinical Development)	25-Jul-2019
PPD Clinical Investigation Lead, Clinical Development Director (Respiratory Therapy Area Unit)	26-Jul-2019
PPD Clinical Development Operations Manager (Respiratory Projects Clinical Platforms and Sciences)	29-Jul-2019
PPD Physician Project Leader, Director (Respiratory Discovery Medicine)	25-Jul-2019
PPD Principal Clinical Data Manager (Respiratory Data Management)	25-Jul-2019

Reviewer	Date
PPD Director (Respiratory Regulatory Affairs)	29-Jul-2019
PPD Director, Respiratory Patient Centered Outcomes (Value Evidence and Outcomes)	29-Jul-2019
PPD Global Medical Affairs Leader, Respiratory (GMAL Trelegy)	27-Jul-2019
PPD Medical Affairs Lead, Respiratory Medical Franchise	29-Jul-2019
PPD Manager, Medical Writing & Clinical Submission Planning	25-Jul-2019
PPD Manager, Medical Writing & Clinical Submission Planning	25-Jul-2019

Clinical Statistics & Clinical Programming Line Approvals
(Method: Pharma TMF eSignature)

Approver	Date
PPD Lead Statistician Line Manager, Senior Statistics Director (Respiratory Clinical Statistics)	30-Jul-2019
PPD Programming Manager (Respiratory Clinical Programming)	30-Jul-2019

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1. INTRODUCTION

NOTE: The RAP may also include any pre-defined analyses for publication purposes.

The purpose of this reporting and analysis plan is to describe the analyses to be included in the Clinical Study Report for Study 207626: A Phase IV, 12-week, randomised, double-blind, double-dummy study to compare single inhaler triple therapy, fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI), with tiotropium monotherapy based on lung function and symptoms in participants with chronic obstructive pulmonary disease (COPD).

Insert revision chronology as detailed within the protocol.

Protocol Revision Chronology:		
2017N323364_00	11-OCT-2017	Original Protocol
2017N323364_01	17-JUL-2018	Protocol amendment 01

2. SUMMARY OF KEY PROTOCOL INFORMATION

Best Practice: Author to copy from the protocol for applicable RAP sections with flexibility to include additional clarification, if required.

Where feasible, every effort should be made to reference the protocol.

Lead RAP author to carefully consider whether information included the RAP would be more beneficial rather than referencing the protocol.

Information contained in this section of the RAP may promote greater clarity in defining the planned analyses for RAP end-users (i.e. CS, CP & RAP Team, outsourced partners or regulatory agencies).

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Detail to Include: Outline & fully justify (where applicable) changes to the planned protocol analysis.

If there are no changes or deviations from the protocol, then specify within this section.

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

Table 1 Changes to Protocol-Defined Analysis Plan

Protocol	Reporting & Analysis Plan	Rationale for Change
Section 10.3 (“Populations for Analysis”) reads in part, “All randomised subjects, excluding those who were randomised in error. A participant who is recorded as a	The verbatim protocol text will be amended in Section 4 of this document to read, “All randomised participants, excluding those who were	Clarification of the definition of “randomized in error.”

Protocol	Reporting & Analysis Plan	Rationale for Change
screen or run-in failure but was also randomised will be considered to be randomised in error. Any other participant who receives a randomisation number will be considered to have been randomised."	randomised in error. A participant who is recorded as a screen or run-in failure and also randomised, but did not receive a dose of study treatment, will be considered to be randomised in error. Any other participant who receives a randomization number will be considered to have been randomised."	
Use of the word "subject."	Text in this document will use the word "participant" in lieu of the word "subject," except in the following cases: 1. In the phrase "subject listing" 2. In the phrase "subject number" 3. In the definition of and abbreviation for the protocol-defined All Subjects Enrolled population 4. Titles and content of prospectively-defined statistical output generated in GSK's HARP system. 5. Use as part of the syntax in the SAS programming language.	Decision by GSK's R&D Clinical Data Standards Board (CDSB), published on GSK's Intranet 18th June 2018. The text below is excerpted from this published notice: Until an industry-wide resolution has been achieved, the R&D Clinical Data Standards Board (CDSB) has decided to continue with the discrepant terminologies and ask teams to: • Data Quality Lead; add a note to the Reviewers Guide in submissions that the term "Subjects" is used to refer to a "Participants" in the protocol. • Statistician to add the same note to RAPs to say that all displays (Tables, Figures & Listings) will use the term 'Subjects'. RAP text will refer to "Participants" in-line *[sic]* with the master RAP template and protocol.
Refinements of descriptions of efficacy analyses.	This document identifies the primary and supplementary estimand, and describes the four attributes of each, the population (Section 7.1.3, , Section 7.3.3), the variable of interest (Section 7.1.1, Section 7.3.1), the intercurrent events of interest (Section 7.1.4, Section 7.3.4), and the summary measure(s) of interest (Section 7.1.2, Section 7.3.2).	Issuance by International Conference on Harmonization of an addendum to the ICH E9 guidance that outlines the concept of the estimand and its four components. Industry adoption of the concepts outlined in this addendum began after finalization of this study protocol.

2.2. Study Objectives and Endpoints

State the study objectives and endpoints **EXACTLY** as specified in the protocol.

Additional clarification may also be included to further describe objectives / endpoints (i.e. if not described in other sections of the RAP). It should be highlighted if this additional information is not in the protocol.

Objectives	Endpoints
Primary Objective	**Primary Endpoint**
To evaluate the effect of single inhaler triple therapy (FF/UMEC/VI) compared to Tiotropium after 12 weeks of treatment on lung function	Change from baseline in trough forced expiratory volume in 1 second (FEV_1) at Week 12 (Day 85)
	Secondary Endpoint
	Changes from baseline in trough FEV_1 at Week 4 (Day 28) and Week 12 (Day 84)
Other Objectives	**Other Endpoints**
To evaluate the effect of single inhaler triple therapy (FF/UMEC/VI) compared to Tiotropium after 12 weeks of treatment on Health Status	• Proportion of responders based on the St George's Respiratory Questionnaire (SGRQ) Total Score at Week 4 and Week 12 • Change from baseline in SGRQ Total Score at Week 4 and Week 12
To evaluate the effect of single inhaler triple therapy (FF/UMEC/VI) compared to Tiotropium after 12 weeks of treatment on Health Status	• Proportion of responders based on the COPD Assessment Test (CAT) Total Score at Week 4 and Week 12 • Change from baseline in CAT Total Score at Week 4 and Week 12
To evaluate the effect of single inhaler triple therapy (FF/UMEC/VI) compared to Tiotropium after 12 weeks of treatment on COPD exacerbations	Moderate or severe exacerbation events
Safety Objective	**Safety Endpoints**
To evaluate the safety profile of single inhaler triple therapy (FF/UMEC/VI) compared to Tiotropium over 12 weeks of treatment	• Incidence of adverse events • Vital signs

2.3. Study Design

Protocol: Reference protocol where applicable and **ONLY** include supportive information.

For example, any elements which may impact or inform the planned analyses or facilitate development, review and execution of the RAP.

Protocol Schematic Recommended: Utilised from the protocol (i.e. use 'cut' option within .pdf version of the protoocl and paste accordingly) but **DO NOT** repeat information which is apparent from the schematic, instead include bulleted points (recommended) or text descriptions to capture key study design information.

Points for Consideration: May include the following (and others as appropriate), so as to aid understanding of statistical methods and elements impacting analyses:

Design Configuration

Experimental Design (e.g. parallel, crossover, factorial, single group, SMART (sequential multiple assignment randomized trial)) and other design elements as required (e.g. dose-escalation, multicentre).

Control Method (e.g. placebo, active comparator, low dose, historical, or none [i.e. uncontrolled]).

Blind Level (e.g. open-label, single-blind, single-blind (sponsor unblinded), double-blind, double-blind (sponsor unblinded), matching placebos, double-dummy).

Sequence and Duration of All Study Periods (e.g. including pre-randomization, single- and double-blind treatment periods, washout, and post-treatment periods)

Sequential Multiple Assignment Randomized Trial (SMART) Designs (e.g. highlights that treatment switch can be built into the study design and doesn't have to be a 'problem' that is solved during analysis. SMARTs eliminate confounding with rescue therapy through sequential randomization. It indirectly highlights that one can compare treatment policies with specific frontline and rescue therapies, and not just perform an ITT analysis.

Copy of Schedule of Events: If included in the Appendix add a link, otherwise delete.

Dosing Information

Dose Regimens in Each Study Period & Stage (e.g. including frequency of administration (e.g., twice daily).

Method & Criteria for Individualizing Dosing (e.g. subject weight or plasma concentrations).

Rules for Dose Changes: Include flexible dosing; modifications in dosage & frequency of dose changes or adjustments; dose reductions, interruptions or tapering and permanent discontinuation for reasons of efficacy or safety (e.g., planned interim analysis with statistical stopping rules or use of an Independent Data Monitoring Committee [IDMC]), re-challenges, and any circumstances for resuming treatment).

Treatment Assignment

Method of Assignment to Treatment (e.g., randomization, stratification, minimisation or specify as appropriate if not randomized and is open label).

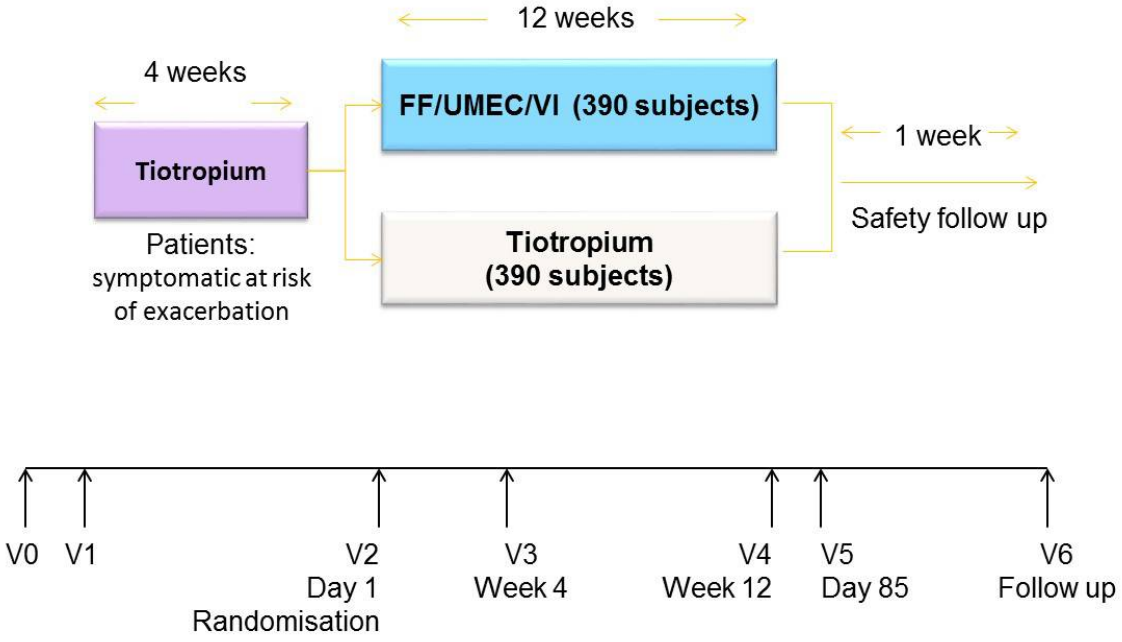
Randomization Procedures (e.g. centralized, site-based or adaptive allocation (i.e. such as assignment on the basis of earlier assignment or outcome).

Method of Generating Randomization Schedule & Assignment (e.g. RandAll NG or other and whether interactive voice response system was used (i.e. RAMOS NG).

Utilisation of Blocking: To maintain blind, **DO NOT** includes the block size.

Adapt & expand accordingly to the study design and apply the principal features illustrated.

Overview of Study Design and Key Features



Design Features	• 12-week treatment period • Randomized • Double-blind • Double-dummy • Parallel-group

Overview of Study Design and Key Features	
	• 1-week safety follow-up • Approximately 848 [participants] with advanced COPD will enter the run-in, in order to randomize approximately 780 [participants], in order to achieve an estimated 702 evaluable [participants]. • A study with 702 evaluable [participants] for the primary analysis will have 90% power to demonstrate superiority of FF/UMEC/VI to tiotropium based on trough FEV_1 at Week 12 (Day 85), at the two-sided 1% significance level, and estimates of residual standard deviation of 240mL and a treatment difference of 70mL. • [Participants] will be provided with short-acting albuterol/salbutamol to be used on an as-needed basis (rescue medication) throughout the study. • [Participants] who permanently discontinue double-blind study treatment are not required to withdraw from the study. [Participants] who have permanently discontinued study treatment and have not withdrawn consent will be encouraged to continue in the study and complete all remaining protocol specified clinic visits as indicated in the Schedule of Activities (Protocol Section 2).
Dosing	Randomized treatments are: • FF/UMEC/VI (100/62.5/25 mcg) via ELLIPTA once daily (QD) in the morning • Tiotropium 18 mcg via HandiHaler QD in the morning
Time & Events	Refer to Section 10.2 ("Appendix 2: Schedule of Activities").
Treatment Assignment	• 4-week run-in on open-label tiotropium (via the HandiHaler) and placebo (via the ELLIPTA) • Randomization 1:1 to FF/UMEC/VI or tiotropium PAREXEL software and Interactive Web Response System (IWRS) will be used to generate the randomization schedule and for treatment allocation. Centralized randomization will be used.
Interim Analysis	No interim analyses are planned.

2.4. Statistical Hypotheses / Statistical Analyses

The primary objective of this study is to compare single inhaler triple therapy (FF/UMEC/VI) with tiotropium in participants with COPD who have received tiotropium and continue to have symptoms as measured by a COPD Assessment Test (CAT) score ≥10. The primary endpoint is the mean change from baseline in trough FEV_1 at Week 12 (Day 85). The primary analysis is the comparison of this endpoint between FF/UMEC/VI and tiotropium.

The null hypothesis is that there is no difference between treatment groups (i.e., H0: T1 – T2 = 0) in the mean change from baseline in trough FEV1 at Week 12 (Day 85), and the alternative hypothesis is there is a difference between treatment groups (i.e., H1: T1 – T2 ≠ 0), where T1 and T2 are the treatment means for FF/UMEC/VI and tiotropium, respectively.

3. PLANNED ANALYSES

3.1. Interim Analyses

No interim analyses are planned.

3.2. Final Analyses

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

1. All participants have completed the study or have been withdrawn as defined in the protocol.
2. All required database-cleaning activities have been completed and final database release has been declared by GSK Data Management.
3. All criteria for unblinding the randomization codes have been met and the final database has been locked.
4. Randomization codes have been distributed per PAREXEL and PAREXEL Informatics' standard operating procedures and treatment details have been unblinded.
5. Database freeze has been declared by GSK Data Management.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Subjects Enrolled (ASE)	All participants for whom a record exists in the study database, including screen failures and any participant who was not screened but experienced an SAE between the date of informed consent and the planned date of the Screening visit.	Study disposition and SAEs for non-randomized participants
Intent-To-Treat (ITT)	All randomised participants, excluding those who were randomised in error. A participant who is recorded as a screen or run-in failure and also randomised but who did not receive any dose of study treatment will be considered to be randomised in error. Any other participant who receives a randomisation number will be considered to have been randomised. Displays will be based on the treatment to which the participant was randomised.	Study Population, Efficacy, Safety

4.1. Protocol Deviations

Important protocol deviations (as defined in the Protocol Deviations Specification Form [PDSF]), include deviations related to study inclusion/exclusion criteria, conduct of the

trial, patient management, and patient assessment. All protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the PDSF.

Data will be reviewed prior to unblinding and freezing the database to ensure that all deviations are captured and categorised on the protocol deviations dataset. This dataset will be the basis for the summaries and listings of protocol deviations.

Important protocol deviations will be summarized by treatment group. A separate summary and listing of all inclusion and exclusion criterion deviations will also be provided. This summary will be based on data recorded on the inclusion/exclusion page of the electronic case report form (eCRF).

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
PAREXEL Informatics Randomization and Trial Management System		Data Displays for Reporting	
Code	Description	Description	Order in output
A	FF/UMEC/VI 100/62.5/25 mcg ELLIPTA	FF/UMEC/VI 100/62.5/25	1
B	Tiotropium 18 mcg HandiHaler	TIO 18	2

Treatment comparisons will be labelled "FF/UMEC/VI 100/62.5/25 vs. TIO 18".

5.2. Baseline Definitions

The baseline value of all endpoints, except as noted in baseline definitions, will be the latest pre-first-dose assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 (Visit 2) assessments are assumed to be taken prior to first dose and will be used as baseline.

Baseline Definitions			
Parameter	Study Assessments Collected prior to dosing		Baseline Definition
	Screening (Visit 1)	Day 1 Pre-Dose (Visit 2)	
Efficacy			
Trough FEV_1 FVC*	X	X	Day 1, defined as the average of the two pre-dose measurements If one of the measurements is missing, then the baseline will be the single remaining value.
SGRQ Total Score		X	Day 1
CAT score	X	X	Day 1
Safety			
Vital signs	X		Most recent individual value prior to first dose (either Screening or a repeat test). Systolic and diastolic blood pressure values should come from the same assessment.
*: FVC is not a protocol specified efficacy endpoint.			

5.3. Multicentre Studies

It is anticipated that approximately 83 sites from the United States and Europe (Poland and the Russian Federation) will participate in the study. Therefore, it is likely that many centres will enrol very small numbers of participants. Consequently, all centres within each country will be pooled.

Enrolment will be summarized and presented by country and centre. "Geographical region" is denoted in the protocol as a covariate in the statistical models assessing several efficacy measures: for the purposes of these analyses, two geographical regions will be defined: Europe (Poland and the Russian Federation) and the United States.

5.4. Examination of Covariates, Other Strata and Subgroups

5.4.1. Covariates and Other Strata

No stratification was used in this study.

Covariates to be included in the statistical analyses as outlined in Section 7 ("Efficacy Analyses") of this document are baseline and geographical region. Additional covariates may also be considered in an *ad hoc* manner at the discretion of the study team, and if considered, would be addressed in the Clinical Study Report.

5.4.2. Examination of Subgroups

No subgroup analyses are planned.

5.5. Multiple Comparisons and Multiplicity

Given that there are only two treatments under consideration in this study, there is only one treatment comparison, that between FF/UMEC/VI and tiotropium.

No multiplicity adjustments are planned for secondary and other endpoints.

5.6. Other Considerations for Data Analyses and Data Handling Conventions

Section Aim: Details have been moved to appendices to facilitate review of the main body of the RAP. If appendices are not relevant for the study, they should be deleted and the list updated.

Flexibility to include details using sub-sections within this section, if required.

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

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

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population summaries will be based on the ITT Population, unless otherwise specified.

Study population summaries of participant disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, and treatment compliance will be based on GSK International Data Standards Library (IDSL) Core Data Standards.

7. EFFICACY ANALYSES

7.1. Primary Efficacy Analyses

The primary efficacy analysis will assess the difference between treatments in the context of superiority of FF/UMEC/VI over tiotropium.

7.1.1. Endpoints / Variables

Where applicable, describe the method for combining measurements to create composite variables. Flexibility to include this information in Appendix 6: Derived and Transformed Data.

The primary efficacy variable is the mean change from baseline in trough FEV_1.

7.1.2. Summary Measure

The summary measure of interest is the adjusted mean treatment difference in trough FEV_1 on Day 85.

7.1.3. Population of Interest

The primary efficacy analyses will be based on the ITT population.

7.1.4. Strategy for Intercurrent (Post-Randomization) Events

Discontinuation of randomized study treatment is considered an intercurrent event for the estimands.

7.1.4.1. Primary estimand

The primary treatment effect to be estimated will be the hypothetical effect if all participants had stayed on their randomised treatment. Trough FEV_1 collected up to the time of treatment discontinuation will be used in the analysis. Trough FEV_1 collected after treatment discontinuation will be set to missing. Missing data will be assumed to be missing at random (MAR).

7.1.4.2. Supplementary estimand

The supplementary treatment effect to be estimated will be the treatment policy effect of initial randomised treatment. All recorded data up to the time of study withdrawal will be included in the analysis, regardless of discontinuation of study treatment. Missing data will be assumed to be MAR. This supplementary treatment effect will only be estimated if >5% of the ITT subjects discontinued the randomized study treatment and have spirometry assessment at Visit 5 .

7.1.5. Statistical Analyses / Methods

Unless otherwise specified, endpoints / variables defined in Section 7.1.1 ("Endpoints / Variables") will be summarised using descriptive statistics, graphically presented (where appropriate), and listed.

Trough FEV_1 will be summarized based on the estimand strategies detailed in Section 7.1.4.1 ("Primary estimand") and Section 7.1.4.2 ("Supplementary estimand").

7.1.5.1. Statistical Methodology Specification

Endpoints / Variables
• Primary endpoint: Change from baseline in trough FEV_1 at Day 85 • Secondary endpoint: Change from baseline in trough FEV1 at Day 28 and Day 84
Model Specification
• The primary model of interest is a mixed model repeated measures (MMRM) analysis, including trough FEV_1 recorded at Day 28, Day 84, and Day 85. The model will include baseline FEV_1, visit, geographical region, and treatment as covariates and visit-by-baseline FEV_1 and visit-by-treatment interaction terms. The visit-by-treatment interaction term is included to allow treatment effects to be estimated at each visit separately. • The variance-covariance matrix will be assumed to be unstructured. • While missing data are not explicitly imputed in the primary MMRM analyses, there is an underlying assumption that the data are missing at random. All available on-treatment assessments will be utilized and via modeling of the within-subject correlation structure, the derived treatment differences will be adjusted to take into account missing data. • Two models will be fitted; one with a response variable of trough FEV_1, and one with a response variable of change from baseline in trough FEV_1. • The model will utilize the OBSMARGINS (OM) option to generate a dataset with a row for every participant-visit combination that contains all the covariates and a macro variable containing the mean baseline for the participants included in the analysis. This is used to derive the adjusted means using coefficients which are based on the participants in the analysis.
Model Checking & Diagnostics
• The Kenward and Roger method (KR) for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used. In the event the model fails to run using the KR method, then the residual method will be used instead. • Distributional assumptions underlying the model used for analysis will be examined by generating a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable. These plots will not be included as part of the statistical output detailed in Section 10.9 (Appendix 9: List of Data Displays).
Model Results Presentation
• Least square (LS) means and LS mean changes from baseline with their corresponding standard errors and 95% confidence intervals (CIs) will be presented for each treatment by visit, together with

estimated treatment differences (FF/UMEC/VI vs. TIO) and the corresponding 95% CIs and p-values.

- A plot of LS mean changes from baseline and 95% CIs from the model will be generated for each treatment by visit.

Subgroup Analyses

No subgroup analyses are planned.

Supportive Analyses - Interactions

The interactions between treatment and other factors will be investigated in the primary analysis as follows by adding interaction terms to the statistical model:

- An assessment of whether the effect of treatment on trough FEV_1 is modified by either geographic region or baseline FEV_1 will be made by fitting separate repeated measures models, identical to the primary analysis models described above but also including additional terms as described below.
  - The primary analysis model will be used with an additional treatment-by-geographical region interaction term and a treatment-by-geographical region-by visit interaction term. The p-value for the treatment-by-geographical region interaction at Day 85 will be computed using contrast statements. If that p-value is ≥ 0.10 then the interaction will be considered not to be statistically significant. If the p-value is < 0.10, further investigation will be undertaken, for example by running the primary analysis by geographic region.
  - The primary analysis model will be used with an additional treatment-by-baseline FEV_1 interaction term and a treatment-by-baseline FEV_1-by-visit interaction. The p-value for the treatment-by-baseline interaction at Day 85 will be obtained using contrast statements. If that p-value is ≥ 0.10 then the interaction will be considered to be not statistically significant. If the p-value is < 0.10, further investigation will be undertaken, for example by running the analysis by dichotomous categories of baseline FEV_1 values (values above and below the median).

Sensitivity and Supportive Analyses

If the overall rate of discontinuation from study treatment is > 5%, a sensitivity analysis for the supplementary estimand (i.e., the Treatment Policy estimand) will be undertaken to address the statistical assumptions made in the primary analysis regarding missing data and the primary statistical hypothesis. This sensitivity analysis of the Treatment Policy estimand of trough FEV_1 on Day 85 will be conducted as follows:

A "tipping point" sensitivity analysis of trough FEV_1 at Day 85 will be undertaken for the ITT Population. This analysis will explore the impact of missing data by using differing assumptions regarding the mean treatment effect in participants who discontinue study treatment. Mean treatment effects investigated will range from a change from baseline trough FEV_1 of -150 mL to +150 mL in increments of 50 mL. For each value of the assumed mean change from baseline for FF/UMEC/VI, the full range of values for the assumed mean change from baseline for Tio will be investigated, thus including scenarios where participants who discontinue FF/UMEC/VI have a lower treatment effect than those who discontinue Tio and vice versa. The analysis results will be used to explore the conditions under which the conclusion of superiority no longer holds.

For each participant with missing data at Day 85, a value will be imputed based

on a random draw from a normal distribution with mean equal to the corresponding assumed mean change from baseline and standard deviation taken from the observed change from baseline data for the combined treatment arms at the Day 85 visit. Data for participants with missing baseline values will not be imputed. Analysis of the complete Day 85 dataset will be carried out using an ANCOVA model with covariates of treatment group, geographical region, region and baseline. A table will be produced displaying the p-values for the treatment difference at Day 85 under the above assumptions for the mean changes from baseline in each treatment arm.

7.2. Secondary Efficacy Analyses

A single statistical model will include data from Days 28, 84, and 85, hence evaluation of the secondary efficacy variables of trough FEV_1 on Days 28 and 84 will be incorporated into the primary efficacy analysis. See Section 7.1 ("Primary Efficacy Analyses") for details.

7.3. Other Efficacy Analyses

The following efficacy analysis will assess the difference between treatments in the context of superiority of FF/UMEC/VI over tiotropium.

7.3.1. Endpoints / Variables

The following endpoints will be used to assess the superiority of FF/UMEC/VI over tiotropium:

- SGRQ total score
- Proportion of population identified via SGRQ total score as responders
- CAT score
- Proportion of population identified via CAT score as responders
- Moderate / severe COPD exacerbations

7.3.2. Summary Measure

The proportions of participants identified as responders based on the SGRQ total score and CAT score at Day 28 and Day 84 will be summarized and analysed by visit and treatment group.

Mean values and changes from baseline in SGRQ total score and CAT score on Days 28 and 84 will be summarized by visit and treatment in terms of summary statistics including means, standard deviations, medians, minima, 1st and 3rd quartiles, and maxima. The treatment comparison of FF/UMEC/VI to tiotropium will be assessed in terms of the mean treatment difference at Day 28 and Day 84.

COPD exacerbations will be summarized by treatment in terms of incidence of on-treatment and post-treatment events.

7.3.3. Population of Interest

The summaries and analyses of SGRQ and CAT data and their associated responder summaries and analyses, as well as the summaries of exacerbation incidence, will be based on the ITT population.

7.3.4. Strategy for Intercurrent (Post-Randomization) Events

All endpoints will use the same strategy for intercurrent events as defined in Section 7.1.4 for the primary estimand.

7.3.5. Statistical Analyses / Methods

Relevant displays will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints and variables defined in Section 7.3.1 will be summarised using descriptive statistics, graphically presented (where appropriate), and listed.

7.3.5.1. Statistical Methodology Specification

7.3.5.1.1. SGRQ total score and CAT score

Endpoint / Variables
• Change from baseline in SGRQ total score at Days 28 and 84. • Change from baseline in CAT score at Days 28 and 84.
Model Specification
• Similar model to that described above in Section 7.1.5.1 (“Statistical Methodology Specification”) for the primary efficacy analysis. • Two models will be fitted; one with a response variable of SGRQ total score/CAT score and one with a response variable of change from baseline in SGRQ total score/CAT score.

7.3.5.1.2. Responder according to SGRQ and CAT score

Endpoint / Variables
• Proportion of responders according to SGRQ total score at Days 28 and 84. • Proportion of responders according to CAT score at Days 28 and 84.
Model Specification
• The proportions of responders as determined by SGRQ total score/CAT score will be analyzed using a generalized linear mixed mode. The model will include terms for baseline score, geographical region, treatment, visit, and visit by baseline and visit by treatment interactions. TIO will be used as the reference level for treatment. • The model will be fit with an unstructured variance-covariance matrix with a single model to include all visits (Days 28 and 84). • Computation of CIs for the odds ratios will be based on the individual Wald tests. • See Section 10.7.2.3 (“Handing of Missing Data for Statistical Analysis”) for details on how to handle missing data.
Model Checking & Diagnostics
• Pearson residuals will be plotted by using PLOTS=RESIDUALPANEL option for the model statement in SAS.
Model Results Presentation
• The number and percentage of responders and non-responders at each visit will be summarized by treatment group. The odds ratio, 95% CI, and p-value will be presented for FF/UMEC/VI vs. tiotropium

7.3.5.1.3. Exacerbations

Endpoint
Incidence of moderate/severe exacerbations.
Model Specification
No formal statistical model is proposed. The annual raw exacerbation rate, together with the total treatment exposure, will be summarized by treatment group. Details of the exacerbations will also be summarized by treatment group and will include the following elements: • the number and percent of participants reporting an exacerbation, both overall and by severity (mild, moderate, severe, and moderate/severe) • number and percent of participants by number of moderate/severe exacerbations (0, 1, ≥2), • frequency distribution of treatment for the exacerbation • frequency distribution of severity • frequency distribution of outcome • simple summary of the duration of the exacerbation On- and post-treatment exacerbations will be summarized separately.

8. SAFETY ANALYSES

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

8.1. Adverse Events Analyses

Adverse events (AEs) analyses will be based on GSK Core Data Standards.

Serious adverse events (SAEs) associated with study participation will be collected from the point of informed consent onward. All AEs, including all SAEs, will be collected starting from randomization, and will be summarised and displayed by randomised treatment group. The onset date of the adverse events relative to the blinded treatment start and stop dates will be used to determine in which period an adverse event occurs.

The AE text recorded in the eCRF will be coded using the Medical Dictionary for Regulatory Activities (MedDRA), and will be reported using the primary System Organ Class (SOC) and Preferred Term (PT). The number of participants with one or more events of any type will be calculated. Results will be displayed in the order of decreasing frequency, both across SOC and within SOC. A SOC will not be included if no AEs in that SOC are reported. If the total incidence for any two or more AEs is equal, the events will be presented in alphabetical order.

Adverse events will also be listed, with SOC, event (preferred term), treatment group, number of participants with the event, and specific subject numbers. Demographic details (e.g. age, gender and race), as well as details of the individual adverse events, will be included in these listings. Listings will be sorted within participant by the date of onset of the AE.

The following by-treatment AE summaries will be provided:

- On-treatment AEs
- Post-treatment AEs
- On-treatment drug-related AEs
- Pre-treatment SAEs
- On-treatment SAEs
- Post-treatment SAEs
- On-treatment fatal AEs
- On-treatment drug-related SAEs
- Pre-treatment SAEs leading to withdrawal from study
- On-treatment AEs leading to withdrawal from study
- On-treatment AEs leading to discontinuation of study treatment
- On-treatment AEs of special interest (AESI)
- On-treatment common non-serious AEs
- 10 most frequent on-treatment AEs in each treatment group
    - In case of ties in frequency, all AEs of that frequency will be displayed
- Standard summary for Food and Drug Administration Amendments Act (FDAAA) report
- Standard summary for European Clinical Trials Database (EudraCT) report

In addition, the following listings of AE data will be provided:

- Subject numbers for all AEs
- Subject numbers for AESI
- All AEs
- Non-fatal SAEs
- Fatal AEs
- AEs leading to withdrawal from study
- AEs leading to discontinuation of study treatment
- Criteria for determining SAEs

8.2. Adverse Events of Special Interest Analyses

The table in Section 10.6.4 ("Safety") presents the groups of Adverse Events of Special Interest (AESI). Groups which are not standardized MedDRA queries comprise a selection of PTs defined by GSK. The complete list, including the PTs that contribute to each of the groups, will be provided by Safety and Medical Governance using the MedDRA version current at the time of reporting. This list will be finalized prior to unblinding.

A comprehensive list of MedDRA terms based on clinical review will be used to identify each type of event. Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting. Furthermore, emerging data from on-going studies may highlight additional adverse events of special interest. Therefore, the list of terms to be used for each event of interest and the specific events of interest will be based on the safety review team (SRT) agreements in place at the time of reporting.

8.3. Other Safety Analyses

Summary statistics of vital signs collected at Visit 1 (Screening) and Visit 4 (Week 12), and change from screening baseline values will be presented by treatment group. Vital signs collected at the Study Treatment Discontinuation Visit and on the Pneumonia Details eCRF form will be included in 'minimum/maximum post-baseline' summaries but will not be summarized separately.

On- and post-treatment bone fractures collected on the Fractures Details eCRF form and on- and post-treatment pneumonia assessments collected on the Pneumonia Details eCRF form will be summarised separately by treatment group. A summary of chest x-rays (on- and post-treatment) will include data from the Exacerbation Chest X-ray and Pneumonia Chest X-ray eCRF pages.

12-lead ECG findings (normal, abnormal – not clinically significant, abnormal – clinically significant) collected at Visit 1 (Screening) will be summarized with frequency distributions by treatment group. Screening lab results will be summarised with descriptive statistics by treatment group.
Any pregnancies reported during the study will be summarized in CSR 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. REFERENCES

GlaxoSmithKline Document Number 2017N323364_00, 207626, A Phase IV, 12 week, randomised, double-blind, double-dummy study to compare single inhaler triple therapy, fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI), with tiotropium monotherapy based on lung function and symptoms in participants with chronic obstructive pulmonary disease, 11-OCT-2017

GlaxoSmithKline Document Number 2017N323364_01, 207626, A Phase IV, 12 week, randomised, double-blind, double-dummy study to compare single inhaler triple therapy, fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI), with tiotropium monotherapy based on lung function and symptoms in participants with chronic obstructive pulmonary disease, 17-JUL-2018

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

Kon, SS, et al. Minimum clinically important difference for the COPD Assessment Test: a prospective analysis. Lancet Respir Med. 2014;2(3):195-203.

Meguro M, Barley EA, Spencer S, Jones PW. Development and validation of an improved COPD-Specific Version of the St. George Respiratory Questionnaire. Chest 2007;132(2):456-63.

10. APPENDICES

10.1. Appendix 1: Protocol Deviation Management

No Per-Protocol Population is defined in this study; hence, no data will be excluded from planned analyses due to protocol deviations. However, protocol deviations will be monitored during the study, and important protocol deviations will be identified as detailed in the Protocol Deviation Specification Form prior to reporting. Details of the summary and listing of protocol deviations can be found in Section 4.1 ("Protocol Deviations").

10.2. Appendix 2: Schedule of Activities

Protocol Activity	Pre-Screen	Screen		Treatment			Follow-up	
	Visit 0	Visit 1 Screen / Run-in	Visit 2 Randomization	Visit 3	Visit 4	Visit 5	Study Treatment Discontinuation Visit	Visit 6 Safety Follow-up Contact
Study Day	**Day -56 to -28**	**Day- 28**	**Day 1**	**Day 28**	**Day 84**	**Day 85**		**Day 91**
Week	**-8 to -4**	**-4**	**0**	**4**	**12**	**12**		**13**
Window		**-3 / +8d (Day -31 to -21)**		**-4 / +2d (Day 24 to 30)**	**-4 / +2d (Day 80 to 86)**			**-1 / +4d (Day 90 to 95)**
Written Informed Consent [a]	X	X						
Genetic Informed Consent [b]	X	X						
Demography [c]	X	X						
Medical History, including cardiovascular history		X						
COPD and Exacerbation History		X						
Concomitant Medication Assessment	X	X	X	X	X		X	X
Inclusion/Exclusion Criteria		X	X					
Smoking History		X						
Smoking status		X			X		X	
Smoking Cessation Counselling		X			X		X	
Register Visit in IWRS	X	X	X	X	X		X	X
CAT [d]		X	X	X	X			
SGRQ-C [d]			X	X	X			
Reversibility Testing [e]		X						
Trough Spirometry [f]			X	X	X	X		
Device training and registration		X	X					
Exacerbation Assessment		X	X	X	X		X	X
Physical examination [g]		X			X		X	
Adverse Events Assessment		X	X	X	X		X	X
Vital signs [h]		X			X		X	
ECG		X						
Chest X-ray [i]		X						

Protocol Activity	Pre-Screen	Screen		Treatment			Follow-up	
	Visit 0	Visit 1 Screen / Run-in	Visit 2 Randomization	Visit 3	Visit 4	Visit 5	Study Treatment Discontinuation Visit	Visit 6 Safety Follow-up Contact
Oropharyngeal examination		X	X	X	X		X	
Blood Draw for Genetics research [j]			X					
Hematology/biochemistry [k]		X						
Urine Pregnancy Test [l]		X			X		X	
Hepatitis B and C tests		X						
Dispense run-in treatment		X						
Dispense study treatment			X	X				
Administer run-in treatment in clinic [m]		X						
Administer study treatment in clinic [n]			X	X	X			
Assess run-in treatment compliance			X					
Collect run-in treatment			X					
Assess study treatment compliance				X	X		X	
Collect study treatment				X	X		X	
Dispense albuterol/salbutamol		X	X	X	X			
Collect albuterol/salbutamol			X	X	X	X	X	
Dispense paper Medical Problems worksheet	X	X	X	X	X			
Review paper Medical Problems worksheet		X	X	X	X	X	X	

a. Informed consent must be conducted at the Pre-screen Visit prior to performing any study procedures including the changing or withholding of medications. The informed consent may be given at Screening Visit 1 if the participant does not take or has not taken any protocol excluded medications. The Pre-screen and Screening Visits can occur on the same day.

[b.] Genetics research consent may be obtained at the same time as the study informed consent and must be obtained prior to obtaining a genetic blood sample. The sample can be collected at any time after Visit 2, providing consent is obtained.

[c.] Demography may be captured at either the Pre-screen Visit or Screening Visit.

[d.] SGRQ-C and CAT will be completed electronically, and should be conducted in the following order and before other study assessments: CAT, SGRQ-C.

[e.] At Screening Visit 1 both pre- and post-bronchodilator spirometry will be conducted. Participants are required to withhold their usual morning doses of their COPD meds including rescue albuterol/salbutamol for the protocol designated period prior to reversibility testing.

[f.] Pre-bronchodilator spirometry will be performed pre-dose at 30 mins and 5 mins prior to taking the morning dose of study treatment, between 6am and 11am and after withholding rescue albuterol/salbutamol for ≥4 hours. On Day 85, study drug will not be administered following spirometric assessments.
[g.] Physical examination may include height, weight, blood pressure and temperature.
[h.] Vital signs must be performed prior to spirometry and prior to taking morning dose of study treatment.
[i.] Chest X-ray is required at Screening (or historical x-ray obtained within 3 months prior to Screening) and at any time there is a suspected pneumonia or a mod/severe exacerbation.
[j.] Genetic consent must be obtained prior to obtaining a blood sample.
[k.] Hematology and chemistry panels will include full and differential blood count and liver chemistry. See Appendix 8 of the protocol.
[l.] All female participants of child bearing potential will have a urine pregnancy test at Visits 1, 4 and Study Treatment Discontinuation Visit (if applicable).
[m.] Participants must withhold their morning dose of existing COPD medication/study treatment and not take their treatment until instructed to do so by study staff.
[n.] Participants must withhold their morning dose of study treatment at each clinic visit and not take their study treatment until instructed to do so by study staff.

When multiple assessments and procedures are performed, suggested order is CAT, SGRQ-C, vitals, ECG, spirometry, clinical lab assessments.

10.3. Appendix 3: Assessment Windows

In instances where multiple measurements have been collected and recorded at the same time point, then the first non-missing value will be used as the assessment associated with that time point.

In general terms, data will be reported per the nominal time of clinic visits and assessments as specified in the protocol. For example, if a participant's recorded values for the Week 4 visit were actually made on the 21st day of treatment, they will be presented as Week 4 values in the summary tables.

Participants that permanently stop study medication early between scheduled clinic visits should undergo all assessments listed for the Study Treatment Discontinuation Visit. Data collected at this visit will be listed and used in summary or analysis tables as part of the 'worst case post- baseline' summary/analysis if appropriate.

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

10.4.1. Study Phases

Assessments and events will be classified per time of occurrence relative to the start and/or stop date of the randomized study treatment. The earliest and latest exposure randomized study treatment start and stop dates will be used to determine whether an assessment or event was pre-treatment, on-treatment or post-treatment. If it is not possible to tell whether an assessment or event was on-treatment, it will be considered as on-treatment. The 'worst case-post baseline' derivation for summaries will consider all scheduled and unscheduled measurements that have been assigned a treatment phase of 'On-treatment'.

10.4.1.1. Study Phases for Concomitant Medication

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

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

Treatment Phase	Definition
Prior to Screening	Medications taken between date of Screening – 90 days and date of Screening (inclusive) defined as: (conmed start date <= date of Screening or 'Taken prior to study?' is 'Yes') and (conmed stop date >= date of Screening – 90 or (conmed stop date is completely missing and date of Screening is non-missing)) Note: this screening data will only be summarized for COPD medications. All screening data will be listed.
Run-in	Medications taken any time between the date of Screening and Treatment Start Date (exclusive) defined as: (conmed start date < randomized treatment start date or randomized treatment not started or conmed start date is missing) and (conmed stop date > date of Screening or (conmed stop date is completely missing and date of Screening is non-missing))
On-treatment	If randomized treatment stop date > randomized treatment start date then this includes medications taken between the randomized treatment start date and randomized treatment stop date - 1 (inclusive) defined as follows: (conmed start date < randomized treatment stop date or conmed start date is missing) and (conmed stop date >= randomized treatment start

Treatment Phase	Definition
	date or (conmed stop date is completely missing and randomized treatment start date is non-missing)) If randomized treatment stop date = randomized treatment start date then this includes medications taken on the randomized treatment start date (which is equal to the randomized treatment stop date) defined as follows. (conmed start date <= randomized treatment stop date or conmed start date is missing) and (conmed stop date >= randomized treatment start date or (conmed stop date is completely missing and randomized reatment start date is non-missing))
Post-treatment	If randomized treatment stop date > randomized treatment start date then this includes medications taken between the date of randomized treatment stop date and the date of study conclusion (inclusive) defined as follows: (conmed start date <= study conclusion date or conmed start date is missing) and (conmed stop date >= randomized treatment stop date or (conmed stop date is completely missing and randomized treatment stop date is non-missing)) If randomized treatment stop date = randomized treatment start date then this includes medications taken between the date of randomized treatment stop date + 1 and the date of study conclusion (inclusive) defined as follows. (conmed start date <= study conclusion date or conmed start date is missing) and (conmed stop date > randomized treatment stop date or (conmed stop date is completely missing and randomized treatment stop date is non-missing))

NOTES:

- A concomitant medication will be classed in every period of the study in which it was taken (e.g., prior to screening, run-in, on- treatment, post-treatment).
- See Section 10.7.2.2 for handling of partial dates.

Details of the handling of partial and missing concomitant medication dates can be found in Section 10.7.2 (“Handling of Missing Data”).

10.4.1.2. Study Phases for Other Data

Any events/assessments for participants not in the ITT population will be assigned a Pre-treatment phase.

For all events and assessments where time is recorded, pre-treatment, on-treatment and post-treatment phases will be defined as below:

Study Phase	Definition
Pre-Treatment	• Event onset date/time or assessment date/time < randomized treatment start date/time
On-Treatment	• Randomized treatment start date/time ≤ event onset date/time or assessment date/time ≤ randomized treatment stop date + 1, or any event/assessment with a missing or partial onset date unless there is evidence it was not on-treatment
Post-Treatment	• Event onset date/time or assessment date/time ≥ randomized treatment stop date + 2, and event onset date/time or assessment date/time ≤ study conclusion date

For all events and assessments (with the exception of concomitant medications, SGRQ and CAT assessments) where time is not recorded, pre-treatment, on-treatment and post-treatment phases will be defined as below:

Study Phase	Definition
Pre-Treatment	• Event onset date or assessment date < randomized treatment start date
On-Treatment	• Randomized treatment start date ≤ event onset date or assessment date ≤ randomized treatment stop date + 1, or any event/assessment with a missing or partial onset date unless there is evidence it was not on-treatment
Post-Treatment	• Event onset date or assessment date ≥ randomized treatment stop date + 2 and event onset date or assessment date ≤ study conclusion date

For SGRQ and CAT assessments, pre-treatment, on-treatment and post-treatment phases will be defined as below:

Study Phase	Definition
Pre-Treatment	• Event onset date or assessment date ≤ randomized treatment start date
On-Treatment	• Randomized treatment start date < event onset date or assessment date ≤ randomized treatment stop date + 1, or any event/assessment with a missing or partial onset date unless there is evidence it was not on-treatment
Post-Treatment	• Event onset date or assessment date ≥ randomized treatment stop date + 2 and event onset date or assessment date ≤ study conclusion date

10.4.2. Treatment-Emergent Flag for Adverse Events and Exacerbations

Flag	Definition
Treatment Emergent	Randomized treatment Start Date ≤ AE Start Date ≤ Randomized treatment Stop Date + 1.

NOTES:

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

10.5. Appendix 5: Data Display Standards & Handling Conventions

10.5.1. Reporting Process

Software	
The currently supported versions of SAS software will be used to program all output described in this document.	
Reporting Area	
HARP Server	uk1salx00175
HARP Compound	gsk2834425/mid207626/final_01
Analysis Datasets	
Analysis datasets will be created according to CDISC standards (SDTM Implementation Guide Version 3.2 (or more recent, if updated after finalization of this document) & Analysis Data Model (ADaM) Implementation Guide Version 1.0 (or more recent, if updated after finalization of this document).	
Generation of RTF Files	
RTF files will be generated from output described in this analysis plan.	

10.5.2. Reporting Standards

General

- All data displays (Tables, Listings and Figures) will use the term "Subject" which reflects CDISC and GSK Data Display Standards terminology.
- 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

- Unless otherwise stated, all results will be reported according to the treatment to which the participant was randomized. However, there may be additional adhoc displays for individual participants using the actual treatment received.
- GSK IDSL Statistical Principles (5.03 & 6.06.3) for precision (i.e., the number of decimal places reported) will be adopted for reporting of data based on the raw data collected.
- Numeric data will be reported at the precision collected on the eCRF or recorded in the raw dataset if from non-eCRF sources.
- The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of decimal places.
- Percentages between 1% and 99%, inclusive, will be rounded to integers. Percentages greater than 0%, but less than 1%, will be reported as <1%, and percentages greater than 99%, but less than 100%, will be reported as >99%.

Planned and Actual Time

- Reporting for tables, figures, and 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 randomized study treatment dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1). Unscheduled or unplanned readings will be included in the data listings.

Unscheduled Visits

- Unscheduled visits will not be included in figures or in summary tables except as a part of a 'minimum/maximum 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 Principles 7.01 to 7.13.

- The programs for statistical analysis tables will create SAS datasets with the unrounded numbers from the statistical models to be used in any graphs. These datasets will include all LS means, standard errors, treatment differences or ratios, and CIs. These analysis datasets will be created for all analysis tables regardless of whether a figure is planned as part of SAC.

10.6. Appendix 6: Derived and Transformed Data

10.6.1. General

Study Day

• Calculated as the number of days from treatment start date (i.e., randomised treatment start date):
  • Reference date = missing → Study day = missing
  • Reference date < treatment start date → Study day = reference date – treatment start date
  • Reference date ≥ treatment start date → Study day = reference date – treatment start date +1

Randomized Treatment Start and Stop Dates
• Randomized treatment start date will be defined as the earliest treatment start date. Randomized treatment stop date will be defined as the latest date of randomized treatment exposure date or date of last dose from treatment discontinuation eCRF page. Treatment stop date will be imputed as study completion date if the date of last dose cannot be confirmed but investigational product is returned at the end of study visit (follow up), or if the date of last dose can be confirmed in protocol deviation log to be after study completion date, or if subject completes the study and did not return the investigational product at Visit 4 and the last dose cannot be confirmed.

10.6.2. Study Population

Demographics
Age
Age is calculated in the Interactive Web Response System (IWRS) and will be imported from the IWRS into the clinical database. The IWRS will use GSK standard IDSL algorithms to calculate age. In accordance with GSK policy, only year of birth is collected in the IWRS. To estimate participant age, a complete birthdate will be estimated by using the year recorded by the IWRS and assigning month and day values of '30JUN.' The birth date will be presented in listings as 'YYYY.' Completely missing dates of birth will remain as missing, with no imputation applied. Consequently, the age of the participant will not be calculated and will remain missing. Age, in whole years, will be calculated based on the Pre-Screening Visit date (or Screening date, if pre-screening is not evaluated).
Age Category
Age categories are based on age at Pre-screening and are defined as: • ≤64 years • 65-74 years • 75-84 years • ≥85 years
Body Mass Index (BMI)
BMI will be calculated in the eCRF as Weight (kg) / Height (m) ^{2}.

Demographics

Race

The high-level Food and Drug Administration (FDA) race categories and designated Asian subcategories are:

1. Black or African Heritage
2. American Indian or Alaska Native
3. Asian
    a. Central/South Asian Heritage
    b. Japanese/East Asian Heritage/South East Asian Heritage
    c. Mixed Asian Heritage (only required if data exist)
4. Native Hawaiian or other Pacific Islander
5. White

These categories and subcategories will be summarized along with all combinations of high-level categories which exist in the data. All the high-level race categories and the Asian subcategories must appear on the display even if there are no participants in a particular category, but combinations that do not exist in the data do not need to be represented. Combinations will be represented as the concatenation of the high-level category terms, e.g., "White & Asian". The designated Asian subcategories will not be summarized as combinations with other categories.

In addition, the standard race categories collected on the eCRF page will be summarized along with categories for mixed race. The categories are:

1. American Indian or Alaska Native
2. Asian - Central/South Asian Heritage
3. Asian – East Asian Heritage
4. Asian – Japanese Heritage
5. Asian – South East Asian Heritage
6. Mixed Asian Heritage (only required if data exist)
7. African American/African Heritage
8. Native Hawaiian or other Pacific Islander
9. White – Arabic/North African Heritage
10. White – White/Caucasian/European Heritage
11. White – Mixed Race
12. Mixed Race

"Asian – Mixed Race" is only used if more than one Asian category, but no non-Asian race, is selected. Similarly, "White – Mixed Race" is only used if both of the White categories and no non-White races are selected. If multiple races of different types are selected, then the overall "Mixed Race" category is used.

A participant will only be represented in a single category. A participant who selects a combination of races will be counted as "Asian – Mixed Race," "White – Mixed Race," or "Mixed Race," but not in each of the constituent terms. Therefore, the counts will add up to the total number of participants with a response, and the percentages will add to 100%.

Participant Disposition

- For Kaplan-Meier plots of study withdrawal over time and discontinuation from study treatment over time, censoring will be performed as follows:
    - For study withdrawal, participants are represented from their Day 1 date to the date of early withdrawal from the study (or date of death). Participants that completed the study are

Participant Disposition
censored at the earliest of the date of completion and Day 85. o For discontinuation from study treatment, participants are represented from their Day 1 date to the date of discontinuation from study treatment (or date of death). Participants that complete study treatment per protocol are censored at the earliest of their study treatment stop date and Day 84.

Cardiovascular Risk Factors
• Participants with at least one of the following current or past medical conditions at Screening will be classed as having a cardiovascular (CV) risk factor. The number of CV risk factors at Screening (0, 1, or >=2) will be derived. • Angina pectoris • Coronary artery disease • Myocardial infarction • Arrhythmia • Congestive heart failure • Hypertension • Cerebrovascular accident • Diabetes mellitus • Hypercholesterolemia
Smoking Status
• Smoking Status at Screening is determined directly from the eCRF. • A participant's smoking status from Visit 2 (Day 1) onwards will be derived from the smoking status at the visit in question and any changes in smoking status from the time of the previous assessment (e.g., date of any changes in status were made). • Only smoking status responses recorded at scheduled visits will be included in the summary tables.

Treatment compliance

If a dose counter start count is missing, then it will be assumed to be 30. If any dose counter stop is missing, then the treatment compliance will be set to missing for that participant and for that inhaler.

Compliance is calculated as follows:

- ELLIPTA compliance = (dose counter start – dose counter stop) x 100 / (exposure stop date – exposure start date +1)
- HandiHaler compliance = (number of capsules dispensed – number of capsules returned) x 100 / (exposure stop date – exposure start date +1)
- Overall Compliance = (compliance for ELLIPTA + compliance for HandiHaler) / 2.

Overall and individual inhaler compliance will be summarized during both the run-in and randomized study treatment periods, and will be categorized as follows:

< 80 %
≥ 80 % to < 95 %
≥ 95 % to ≤105 %
>105 % to ≤120 %
>120 %.

If a participant received a treatment other than the randomized study treatment during the study, the compliance will still be calculated using data from all containers received and overall exposure start and stop dates.

Medical Conditions and Concomitant Medications

COPD Concomitant Medications

- COPD concomitant medications will be grouped into the following RMCs based on pre-defined code lists derived from ATC classifications:
  - Antiinfectives (antibiotics, antifungals, antivirals, antiseptics)
  - Short-acting anticholinergic
  - Short-acting beta-2 agonist
  - Long-acting anticholinergic
  - Long-acting beta-2 agonist
  - Xanthine
  - PDE4 inhibitor
  - Corticosteroid – inhaled
  - Corticosteroid – depot
  - Corticosteroid - systemic oral parenteral and intra-articular
  - Corticosteroid – other
  - Leukotriene receptor antagonist
  - Nedocromil or cromolyn sodium
  - Mucolytic
  - Oxygen
  - Other medication given for exacerbation

Medical Conditions and Concomitant Medications
• Other COPD medication
COPD Medication combination
COPD medications taken on the day of the Screening visit will be grouped into the following categories based on the RMC classification: • ICS • LABA • LAMA • Xanthine • PDE4 Inhibitors • Any combination of the above • Other • None
COPD Exacerbation History
COPD exacerbations reported in the past 12 months will be categorized as 0, 1, 2, ≥3 The number of COPD exacerbations reported in the past 12 months prior to Screening will be summarized in three categories: moderate COPD exacerbations, severe COPD exacerbations, and moderate/severe COPD exacerbations. Moderate COPD exacerbations are defined as exacerbations that required treatment with systemic/oral corticosteroids and/or antibiotics (not involving hospitalization). Severe COPD exacerbations are defined as exacerbations that required in-patient hospitalization. The total number of moderate/severe COPD exacerbations is defined as the total numbers of moderate and severe COPD exacerbations.

Reversibility

• A participant's status as reversible to salbutamol is calculated at Screening and is based on the difference (absolute change and % change) between a participant's pre-salbutamol assessment of FEV_1 and their post-salbutamol assessment FEV_1 and is defined as follows:
  • Reversible, if the difference in FEV_1 was ≥ 12% and ≥ 200 mL, or
  • Non-reversible, if the difference in FEV_1 is < 200 mL or else the difference was ≥ 200 mL and was < 12 % of the pre-salbutamol FEV_1.

GOLD Grade 1-4 at Screening

Participants will be classified into Global Initiative on Obstructive Lung Disease (GOLD) Grades 1-4 using the post-salbutamol percent predicted FEV1 assessment at Screening:
  • GOLD Grade 1 (Mild): percent predicted $FEV_1 \geq 80\%$
  • GOLD Grade 2 (Moderate): $50\% \leq$ percent predicted $FEV_1 < 80\%$
  • GOLD Grade 3 (Severe): $30\% \leq$ percent predicted $FEV_1 < 50\%$
  • GOLD Grade 4 (Very Severe): percent predicted $FEV_1 < 30\%$

10.6.3. Efficacy

Lung Function
On-Treatment Trough FEV_1
For Day 28 ad Day 84, trough FEV_1 is defined as the average of the two pre-dose FEV_1 measurements recorded before the morning dose of randomized study medication. If only one pre-dose measurement is recorded, then it will serve as the trough value. For Day 85, trough FEV_1 is defined as the mean of the two planned spirometry FEV_1 measurements. If only one measurement is recorded, then it will serve as the trough value.
Post-Treatment Trough FEV_1
Post-treatment trough FEV_1 is defined as the mean of the two planned spirometry FEV_1 measurements. If only one measurement is recorded, then it will serve as the trough value.
Patient-Reported Outcomes
St George's Respiratory Questionnaire -- COPD (SGRQ-C) Total Score
The SGRQ-C includes 14 questions with a total of 40 items grouped into three domains (Symptoms, Activity, and Impacts). The details for how to score the SGRQ-C are outlined in the SGRQ-C manual (Jones, 2016). This manual includes details on how to handle missing data. The SGRQ-C total score will be converted to an SGRQ score as described in the manual. The change from baseline in total score will be calculated for the converted scores. If the language of the SGRQ-C assessed at a post-randomization visit is different from the language used at Day 1, all SGRQ-C scores at that visit and all subsequent visits will be set to missing. Missing data will be handled as detailed in the SGRQ-C manual (Jones, 2016).

St George's Respiratory Questionnaire (SGRQ) Responders

SGRQ-C is assessed at randomization and on Days 28 and 84. The SGRQ-C will be scored to produce SGRQ total scores (Jones, 2016). Responder analyses will be based on the resulting SGRQ total scores.

A participant will be considered a responder per the SGRQ if his/her on-treatment SGRQ total score has decreased at least 4 units from the baseline SGRQ total score.

A participant will be considered a non-responder if his/her on-treatment SGRQ total score has decreased by fewer than 4 units, has not changed, or has increased compared to baseline.
The handling of missing data will be detailed in Section 10.7.2.

When determining if a participant was a responder to SGRQ Total Score, the Total Score will be rounded to 1dp prior to assigning the responder status.

COPD Assessment Test (CAT) Score

- The CAT consists of eight items each formatted as a six-point differential scale: 0 (no impact) to 5 (high impact). A CAT score will be calculated by summing the non-missing scores on the eight items with a range from 0 to 40.
- If one item is missing, then the score for that item is set as the average of the non-missing items. If more than one item is missing, then the CAT score will be set to missing.
- If the language of the CAT conducted at a post-baseline visit is different to the language used at Day 1 baseline, the CAT score for that visit and all subsequent visits will be set to missing.

Since the CAT score at screening is a study entry criterion, screening CAT scores will be categorized as less than 10 and 10 or greater, and those categories summarized by treatment group.

COPD Assessment Test (CAT) Responders

A participant will be a considered a responder per the CAT if his/her on-treatment CAT total score has decreased at least 2 units from the baseline CAT score.

A participant will be considered a non-responder if his/her on-treatment CAT score has decreased by fewer than 2 units, has not changed, or has increased compared to baseline.

The handling of missing data will be detailed in Section 10.7.2

COPD Exacerbations

- The duration of the exacerbation will be calculated as (exacerbation resolution date or date of death - exacerbation onset date + 1).
- The time to the first on-treatment exacerbation will be calculated as (exacerbation onset date of first on-treatment exacerbation – date of start of treatment + 1).
- For summaries/analyses, participants will be represented from their Day 1 date to the start date of their first event up to and including their treatment stop date+1 day.
- Participants that have not withdrawn from study treatment or experienced the event are censored at their treatment stop date+1 day.
- The event rate for exacerbations will be calculated as the total number of events divided by the total annual participant exposure during the time-period of interest

10.6.4. Safety

Exposure
Extent of exposure
Duration of exposure to randomized treatment will be calculated as: • Randomized treatment stop date – randomized treatment start date + 1 Duration of post-treatment time spent in the study will be calculated as: • Study conclusion date – randomized treatment stop date Duration of total time spent in the study will be calculated as: • Study conclusion date – randomized treatment start date + 1
Exposure Categories
The following exposure categories will be derived for summaries of the ITT population: • ≥1 day • ≥4 weeks • ≥8 weeks • ≥12 weeks • 11 – 13 weeks.

Adverse Events

AEs of Special Interest

- AESI have been defined as AEs which have specified areas of interest for FF, VI or UMEC or the overall COPD population. The following table presents the AESI groups. Groups which are not SMQs are made up of a selection of preferred terms (PTs) defined by GSK. The complete list, including the PTs which contribute to each of the groups will be provided by Safety and Medical Governance (SMG) using the MedDRA version current at the time of reporting. This will be finalized prior to unblinding.

AESI Group	AESI Subgroup	Sub-SMQ
Cardiovascular effects	Cardiac arrhythmia	Arrhythmia related investigations, signs and symptoms (SMQ)
		Bradyarrhythmia terms, nonspecific (SMQ)
		Conduction defects (SMQ)
		Disorders of sinus node function (SMQ)
		Cardiac arrhythmia terms, nonspecific (SMQ)
		Supraventricular tachyarrhythmias (SMQ)
		Tachyarrhythmia terms, nonspecific (SMQ)
		Ventricular tachyarrhythmias (SMQ)
	Cardiac failure (SMQ)	
	Ischaemic heart disease (SMQ)	
	Hypertension (SMQ)	
	Central nervous system haemorrhages and cerebrovascular conditions (SMQ)	
Decreased bone mineral density and associated fractures		
Pneumonia		Infective pneumonia SMQ (Narrow)
Lower Respiratory Tract Infection (LRTI) excluding pneumonia		

Bone Fracture Incidents

If a participant suffers fractures in multiple locations with the same date of fracture, this event is considered to be one fracture incident.

In the case of multiple fracture types (traumatic/non-traumatic) contributing to one fracture incident, the worst-case fracture type (non-traumatic) will be assigned to the fracture incident. E.g. if a participant has a traumatic wrist fracture and a non-traumatic foot fracture on the same date, this will be considered to be one non-traumatic fracture incident.

Bone fracture incident event rate will be calculated in the same manner as AE rate.

Association of Chest Imaging (X-ray or CT scan) with Pneumonia Event
A chest X-ray is considered associated with pneumonia if it is performed within -7 to +14 days of the date of onset of pneumonia or the date of resolution, whichever date falls later. Details of pneumonia events are collected on the Pneumonia Details eCRF page.

Maximum/Minimum Post-Baseline and Worst-Case Post-Baseline	
Definition	**Reporting Details**
Maximum post-baseline (pulse rate, systolic and diastolic blood pressure)	Maximum on-treatment value over all timepoints
Minimum post-baseline (diastolic blood pressure)	Minimum on-treatment value over all timepoints

NOTES:
The treatment phase definitions to be detailed in the full RAP will be used and only assessments within the on-treatment period will be considered in assessment of maximum/minimum/worst-case post-baseline.

Assessment of maximum/minimum/worst-case post-baseline will include data from scheduled, unscheduled and study treatment discontinuation visits (if applicable). Vital signs (pulse rate, systolic blood pressure and diastolic blood pressure) collected at an assessment associated with a pneumonia event will also be included in derivation of a 'maximum/minimum post-baseline' assessment.

10.7. Appendix 7: Reporting Standards for Missing Data

10.7.1. Premature Withdrawals

Element	Reporting Detail
General	A participant is considered to have completed the study if s/he has completed all phases of the study including pre-screening, screening, run-in, the randomised treatment phase, and the safety follow-up. Withdrawn participants will not be replaced in the study. All available data from participants who are withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

10.7.2. Handling of Missing Data

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

10.7.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in data listings.
Adverse Events, exacerbations, and pneumonia	Missing start day: The first of the month will be used unless it falls before the start date of randomized study treatment, in which case the randomized study treatment start date will be used and hence the event will be considered on-treatment, as defined in Section 10.4 (Appendix 4: Study Phases and Treatment-Emergent Adverse Events). Missing stop day: The last day of the month will be used unless it falls after the stop date of randomized study treatment, in which case the randomized study treatment stop date will be used. Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will also be missing.

10.7.2.2. Handling of Partial Dates

The eCRF allows partial dates (i.e., only month and year) to be recorded for AEs, concomitant medications, and exacerbation start and end dates; that is, the day of the month may be missing. In such cases, the following conventions will be applied for calculating the time to onset and the duration of the event:

Element	Reporting Detail
Concomitant medications	For the purposes of assigning a treatment period in which to report a concomitant medication, partial administration start and stop dates recorded in the CRF will be imputed using the following conventions: If the partial date is a start date, 1 will be used for missing days and 'Jan' will be used for missing months. If the partial date is a stop date, either 28, 29, 30, or 31 (depending on the month and year) will be used for missing days and 'Dec' will be used for missing months. The recorded partial date will be displayed in any relevant listings.
Adverse events, exacerbations, and pneumonia	Any partial dates for adverse events and exacerbations will be raised to data management. If the full date cannot be ascertained, the following assumptions will be made. If the partial date is an onset date, 1 will be used for missing days and 'Jan' will be used for the month. However, if these substitutions result in an onset date prior to Day 1 and, based on available information, the event could possibly have occurred during treatment, then the Day 1 date will be assumed to be the onset date. The event will then be considered to have started on treatment.

Element	Reporting Detail
	If the partial date is a resolution date, either 28, 29, 30, or 31 (depending on the month and year) will be used for missing days and 'Dec' will be used for missing months. The recorded partial date will be displayed in any relevant listings.

10.7.2.3. Handling of Missing Data for Statistical Analysis

Element	Reporting Detail
Responder	• Participants with a missing baseline will have responder status as missing • Participants with missing post-baseline data at a time point and a subsequent non-missing assessment will not be considered a responder or non-responder but will be left as missing at that time point • Participants with a missing post-baseline assessment with no subsequent non-missing assessments will be considered a non-responder for that and all subsequent time points. • Participants with a baseline but all missing post-baseline data will be considered a non-responder at all time points.

10.8. Appendix 8: Abbreviations & Trade Marks

10.8.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse event
AESI	Adverse events of special interest
ASE	All subjects enrolled
ATC	Anatomical therapeutic chemical
CAT	COPD Assessment Test
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CSV	Comma-separated values
CT	Computerized (axial) tomography
DR	Dry run
eCRF	Electronic case record form
ECG	Electrocardiogram
EudraCT	European Union Drug Regulating Authorities Clinical Trials
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
FEV_1	Forced expiratory flow in 1 second
FF	Fluticasone furoate
GOLD	Global Initiative on Obstructive Lung Disease
GSK	GlaxoSmithKline
HARP	Harmonised Analysis and Reporting Platform
ICH	International Conference on Harmonization
ICS	Inhaled corticosteroid
IDSL	Integrated Data Standards Library
ITT	Intent-o-Treat
IWRS	Interactive web response system
KR	Kenward and Roger
LABA	Long-acting $beta_2$ agonist
LAMA	Long-acting muscarinic antagonist
LS	Least squares
LRTI	Lower respiratory tract infection
MAR	Missing at random
mcg	microgram
MedDRA	Medical Dictionary for Regulatory Activities
mL	Milliliter
PDE4	Phosphodiesterase type 4
PDSF	Protocol deviation specification form
QD	*Quaque die* (once daily)
R&D	Research and Development
RAP	Reporting and Analysis Plan

Abbreviation	Description
RMC	Respiratory Medication Classification
RUCAM	Roussel Uclaf Causality Assessment Method
SAC	Statistical analysis complete
SAE	Serious adverse event
SDTM	Study Data Tabulation Model
SGRQ	St George's Respiratory Questionnaire
SGRQ-C	St George's Respiratory Questionnaire - COPD
SI	System Independent
SRT	Safety review team
SOC	System organ class
UMEC	Umeclidinium
VI	Vilanterol

10.8.2. Trademarks

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10.9. Appendix 9: List of Data Displays

10.9.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.37	1.1 to 1.2
Efficacy	2.1 to 2.23	2.1 to 2.10
Safety	3.1 to 3.34	3.1
Section	**Listings**	
ICH Listings	1 to 21	
Other Listings	22 to 48	

10.9.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and, if required, example mock-up displays provided in Section 10.10 (Appendix 10: Example Mock Shells for Data Displays). Output files in the following sections that use standard IDSL examples are identified in the "IDSL / Example Shell" column by their IDSL example format code.

Section	Figure	Table	Listing
Study Population	POP_Fnn	POP_Tnn	POP_Lnn
Efficacy	EFF_Fnn	EFF_Tnn	EFF_Lnn
Safety	SAF_Fnn	SAF_Tnn	SAF_Lnn

10.9.3. Deliverables

Delivery	Description
DR	Dry run prior to source data lock
SAC	Final statistical analysis complete
Post-SAC	One week after SAC

10.9.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Participant Disposition					
1.1.	ASE	POP_T01	Summary of Subject Populations and Reasons for Screen/Run-in Failure		DR, SAC
1.2.	ITT	POP_T02	Summary of Attendance at Each Visit		DR, SAC
1.3.	ITT	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment		DR, SAC
1.4.	ITT	ES1	Summary of Study Status and Reasons for Study Withdrawal		DR, SAC
1.5.	ASE	DM11	Summary of Age Ranges	Use age ranges in Section 10.6.2.	DR, SAC
1.6.	ASE	NS1	Summary of Number of Subjects Enrolled by Geographical Region, Country and Center		DR, SAC
1.7.	ITT	NS1	Summary of Number of Subjects Enrolled by Geographical Region, Country, and Center		DR, SAC
1.8.	ASE	IE1	Summary of Inclusion/Exclusion Criteria Deviations for Screen Failures		DR, SAC
1.9.	ITT	IE1	Summary of Inclusion/Exclusion Criteria Deviations		DR, SAC
Protocol Deviation					
1.10.	ITT	POP_T03	Summary of Important Protocol Deviations		DR, SAC
Demographic and Baseline Characteristics					
1.11.	ITT	DM1	Summary of Demographic Characteristics	Add BMI to IDSL standard	DR, SAC
1.12.	ITT	DM1	Summary of Demographic Characteristics by Country		DR, SAC
1.13.	ITT	DM5	Summary of Race and Racial Combinations		DR, SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.14.	ITT	DM6	Summary of Race and Racial Combinations Details		DR, SAC
Medical Conditions					
1.15.	ITT	MH4	Summary of Current Medical Conditions	Use classes and conditions as collected on eCRF	DR, SAC
1.16.	ITT	MH4	Summary of Past Medical Conditions	Use classes and conditions as collected on eCRF	DR, SAC
1.17.	ITT	POP_T04	Summary of Cardiovascular Risk Factors		DR, SAC
1.18.	ITT	POP_T05	Summary of Family History of Cardiovascular Risk Factors		DR, SAC
Disease Characteristics					
1.19.	ITT	POP_T06	Summary of Smoking History at Screening		DR, SAC
1.20.	ITT	POP_T07	Summary of Smoking Status at Screening		DR, SAC
1.21.	ITT	POP_T08	Summary of COPD History at Screening		DR, SAC
1.22.	ITT	POP_T09	Summary of COPD Exacerbation History at Screening		DR, SAC
1.23.	ITT	POP_T10	Summary of Screening Lung Function		DR, SAC
1.24.	ITT	POP_T10	Summary of Screening Lung Function by Country		DR, SAC
1.25.	‘ITT	POP_T11	Summary of Reversibility and GOLD Grade (1 – 4) at Screening		DR, SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.26.	ITT	POP_T12	Summary of CAT Score and CAT Category at Screening		DR, SAC
Prior and Concomitant Medications					
1.27.	ITT	POP_T13	Summary of COPD Concomitant Medications Taken Prior to Screening	Include total column; use Respiratory Medicines Classification (RMC) level 1 as top-level classification; see MID200812 Table 1.34 (	DR, SAC
1.28.	ITT	POP_T14	Summary of COPD Concomitant Medication Combinations Taken at Screening	Include total column; use RMC as top-level classification; see CTT1166855 Table 1.67 (in SAFIRE)	DR, SAC
1.29.	ITT	POP_T13	Summary of COPD Concomitant Medications Taken during Run-in for Reasons other than an Exacerbation	Include total column; use RMC as top-level classification; see MID200812 Table 1.34	DR, SAC
1.30.	ITT	POP_T15	Summary of On-Treatment COPD Concomitant Medications Taken for Reasons other than an Exacerbation	Include total column; use RMC as top-level classification; see MID200812 Table 1.35	DR, SAC
1.31.	ITT	POP_T15	Summary of Post-treatment COPD Concomitant Medications Taken for Reasons other than an Exacerbation	Include total column; use RMC as top-level classification; see MID200812 Table 1.36	DR, SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.32.	ITT	POP_T13	Summary of Concomitant Medications Taken during Run-in for an Exacerbation	Include total column; use RMC as top-level classification; see MID200812 Table 1.37	DR, SAC
1.33.	ITT	POP_T15	Summary of On-Treatment Concomitant Medications Taken for an Exacerbation	Include total column; use RMC as top-level classification; see MID200812 Table 1.38	DR, SAC
1.34.	ITT	POP_T15	Summary of Post-Treatment Concomitant Medications Taken for an Exacerbation	Include total column; use RMC as top-level classification; see MID200812 Table 1.39	DR, SAC
1.35.	ITT	POP_T16	Summary of On-Treatment Non-COPD Concomitant Medications	Include total column; use ATC level 1 as top-level classification; see MID200812 Table 1.40	DR, SAC
1.36.	ITT	POP_T16	Summary of Post-Treatment Non-COPD Concomitant Medications	Include total column; use ATC level 1 as top-level classification; see MID200812 Table 1.41	DR, SAC
Treatment Compliance					
1.37.	ITT	POP_T17	Summary of Treatment Compliance (%)	See CTT116855 Table 1.75 (in SAFIRE)	DR, SAC

10.9.5. Study Population Figures

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Participant Disposition					
1.1.	ITT	POP_F01	Kaplan-Meier Plot of Time to Study Withdrawal		DR, SAC
1.2.	ITT	POP_F01	Kaplan-Meier Plot of Time to Study Treatment Discontinuation		DR, SAC

10.9.6. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Spirometry					
2.1.	ITT	EFF_T01	Summary of Baseline FEV_1 (L)		DR, SAC
2.2.	ITT	EFF_T01	Summary of Baseline FEV_1 (L) by Country		DR, SAC
2.3.	ITT	EFF_T02	Summary of Trough FEV_1 (L) - Hypothetical Estimand	Includes Days 28, 84, and 85	DR, SAC
2.4.	ITT	EFF_T02	Summary of Trough FEV_1 (L) – Treatment Policy Estimand	Only if overall rate of discontinuation from study treatment is >5%	DR, SAC
2.5.	ITT	EFF_T02	Summary of Trough FEV_1 (L) by Country – Hypothetical Estimand	Includes Days 28, 84, and 85	DR, SAC
2.6.	ITT	EFF_T02	Summary of Trough FEV_1 (L) by Country – Treatment Policy Estimand	Only if overall rate of discontinuation from study treatment is >5%	DR, SAC
2.7.	ITT	EFF_T03	Analysis of Trough FEV_1 (L) - Hypothetical Estimand	Includes Days 28, 84, and 85	DR, SAC
2.8.	ITT	EFF_T03	Analysis of Trough FEV_1 (L) – Treatment Policy Estimand	Only if overall rate of discontinuation from study treatmentis >5%	DR, SAC
2.9.	ITT	EFF_T04	Significance Levels for Interactions of Treatment with Geographical Region and Baseline FEV_1 for Analysis of Trough FEV_1 (L) on Day 85 - Hypothetical Estimand	Includes Days 28, 84, and 85	DR, SAC
2.10.	ITT	EFF_T04	Significance Levels for Interactions of Treatment with Geographical Region and Baseline FEV_1 for Analysis of Trough FEV_1 (L) on Day 85 - Treatment Policy Estimand	Only if overall rate of discontinuation from study treatment is >5%	DR, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.11.	ITT	EFF_T05	Tipping Point Sensitivity Analysis: Two-Sided P-values after Imputing Varying Day 85 Mean Change from Baseline Trough FEV_1 (L) – Treatment Policy Estimand	Only if overall rate of discontinuation from study treatment is >5%. Add * before each p-value that is less than 0.050	DR, Post-SAC
SGRQ					
2.12.	ITT	EFF_T06	Summary of Baseline SGRQ Total and Domain Scores		DR, SAC
2.13.	ITT	EFF_T02	Summary of SGRQ Total and Domain Scores – Hypothetical Estimand		DR, SAC
2.14.	ITT	EFF_T03	Analysis of SGRQ Total Score – Hypothetical Estimand		DR, SAC
2.15.	ITT	EFF_T07	Summary and Analysis of Proportion of Responders as Defined by SGRQ Total Score – Hypothetical Estimand		DR, SAC
CAT Scores					
2.16.	ITT	EFF_T06	Summary of Baseline CAT Score		DR, SAC
2.17.	ITT	EFF_T02	Summary of CAT Score – Hypothetical Estimand		DR, SAC
2.18.	ITT	EFF_T03	Analysis of CAT Score – Hypothetical Estimand		DR, SAC
2.19.	ITT	EFF_T07	Summary and Analysis of Proportion of Responders as Defined by CAT Score – Hypothetical Estimand		DR, SAC
COPD Exacerbations					
2.20.	ITT	EFF_T08	Summary of On-Treatment COPD Exacerbations		DR, SAC
2.21.	ITT	EFF_T09	Summary of On-Treatment Details of COPD Exacerbations		DR, SAC
2.22.	ITT	EFF_T08	Summary of Post-Treatment COPD Exacerbations		DR, SAC
2.23.	ITT	EFF_T09	Summary of Post-Treatment Details of COPD Exacerbations		DR, SAC

10.9.7. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Spirometry					
2.1.	ITT	EFF_F01	Box Plot of Change from Baseline in Trough FEV_1 (L) on Day 85 – Hypothetical Estimand	Might be able to squeeze all three timepoints onto one graph – would be six box plots.	DR, SAC
2.2.	ITT	EFF_F02	Empirical Distribution Function Plot of Change from Baseline in Trough FEV1 (L) on Day 85 – Hypothetical Estimand		DR, SAC
2.3.	ITT	EFF_F03	Least Squares Mean (95% CI) Change from Baseline in Trough FEV1 (L) – Hypothetical Estimand		DR, SAC
2.4.	ITT	EFF_F01	Box Plot of Change from Baseline in Trough FEV_1 (L) on Day 85 – Treatment Policy Estimand	Might be able to squeeze all three timepoints onto one graph – would be six box plots.	DR, SAC
2.5.	ITT	EFF_F02	Empirical Distribution Function Plot of Change from Baseline in Trough FEV1 (L) on Day 85 – Treatment Policy Estimand		DR, SAC
2.6.	ITT	EFF_F03	Least Squares Mean (95% CI) Change from Baseline in Trough FEV_1 (L) – Treatment Policy Estimand		DR, SAC
SGRQ					
2.7.	ITT	EFF_F02	Empirical Distribution Function Plot of Change from Baseline in SGRQ Total Score on Day 84 – Hypothetical Estimand		DR, SAC
2.8.	ITT	EFF_F03	Least Squares Mean (95% CI) Change from Baseline in SGRQ Total Score – Hypothetical Estimand		DR, SAC
CAT Score					
2.9.	ITT	EFF_F02	Empirical Distribution Function Plot of Change from Baseline in CAT Score on Day 84 – Hypothetical Estimand		DR, SAC
2.10.	ITT	EFF_F03	Least Squares Mean (95% CI) Change from Baseline in CAT Score – Hypothetical Estimand		DR, SAC

10.9.8. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Exposure					
3.1.	ITT	SAF_T01	Summary of Treatment Exposure		DR, SAC
Adverse Events (AEs)					
3.2.	ITT	AE13	Overview of On-Treatment Adverse Events		DR, SAC
3.3.	ITT	AE1	Summary of On-Treatment Adverse Events		DR, SAC
3.4.	ITT	AE1	Summary of On-Treatment Adverse Events by Country		DR, SAC
3.5.	ITT	AE1	Summary of Post-Treatment Adverse Events		DR, SAC
3.6.	ITT	AE1	Summary of On-Treatment Drug-Related Adverse Events		DR, SAC
3.7.	ITT	AE15	Summary of On-Treatment Common (>=3% in Either Treatment Group) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		DR, SAC
3.8.	ITT	AE3	Summary of the 10 Most Frequent On-treatment Adverse Events in each Treatment Group	For each treatment group, use number of events without tie-breaker to determine the 10 most frequent AEs	DR, SAC
3.9.	ITT	AE5A	Summary of On-Treatment Adverse Events by System Organ Class and Maximum Intensity		DR, SAC
3.10.	ASE	AE2	Relationship of Adverse Event System Organ Class, Preferred Term and Verbatim Text		DR, SAC
Serious and Other Significant Adverse Events					
3.11.	ASE	AE1	Summary of Pre-Treatment Serious Adverse Events		DR, SAC
3.12.	ITT	AE1	Summary of Pre-Treatment Serious Adverse Events		DR, SAC
3.13.	ITT	AE1	Summary of On-Treatment Serious Adverse Events		DR, SAC
3.14.	ITT	AE1	Summary of On-Treatment Fatal Serious Adverse Events		DR, SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.15.	ITT	AE1	Summary of Pre-Treatment Serious Adverse Events Leading to Withdrawal from Study		DR, SAC
3.16.	ITT	AE1	Summary of On-Treatment Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study		DR, SAC
3.17.	ITT	AE1	Summary of Serious Adverse Events (Serious, Drug-Related Serious, Fatal and Drug-Related Serious) by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		DR, SAC
3.18.	ITT	AE1	Summary of On-Treatment Drug-Related Serious Adverse Events		DR, SAC
3.19.	ITT	AE1	Summary of On-Treatment Drug-Related Fatal Serious Adverse Events		DR, SAC
3.20.	ITT	AE1	Summary of On-Treatment Adverse Events of Special Interest		DR, SAC
3.21.	ITT	AE1	Summary of On-Treatment Serious Adverse Events of Special Interest		DR, SAC
3.22.	ITT	AE1	Summary of Post-Treatment Serious Adverse Events		DR, SAC
3.23.	ITT	AE1	Summary of Post-Treatment Serious Fatal Adverse Events		DR, SAC
Pneumonia					
3.24.	ITT	SAF_T02	Summary of On-Treatment Pneumonia Incidence		DR, SAC
3.25.	ITT	SAF_T03	Summary of On-Treatment Details of Pneumonia		DR, SAC
3.26.	ITT	SAF_T02	Summary of Post-Treatment Pneumonia Incidence		DR, SAC
3.27.	ITT	SAF_T03	Summary of Post-Treatment Details of Pneumonia		DR, SAC
Bone fractures					
3.28.	ITT	SAF_T04	Summary of On-Treatment Bone Fractures		DR, SAC
3.29.	ITT	SAF_T04	Summary of Post-Treatment Bone Fractures		DR, SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Chest imaging					
3.30.	ITT	SAF_T05	Summary of Chest Imaging (X-Ray or CT Scan)	combine on- and post-treatment	DR, SAC
Labs					
3.31.	ITT	SAF_T06	Summary of Blood Chemistry Results at Screening		DR, SAC
3.32.	ITT	SAF_T06	Summary of Hematology Results at Screening		DR, SAC
Vital signs					
3.33.	ITT	SAF_T07	Summary of Vital Signs		DR, SAC
3.34.	ITT	SAF_T07	Summary of Change from Baseline Vital Signs		DR, SAC
ECGs					
3.35.	ITT	SAF_T08	Summary of ECG Findings at Screening		DR, SAC

10.9.9. Safety Figures

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Exposure					
3.1.	ITT	SAF_F01	Summary of Treatment Exposure		DR, SAC

10.9.10. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.	ASE	ES7	Listing of Reasons for Screening / Run-in Failure		DR, SAC
2.	ITT	TA1	Listing of Planned and Actual Treatments		DR, SAC
3.	ITT	SD2	Listing of Reasons for Study Treatment Discontinuation		DR, SAC
4.	ITT	ES2	Listing of Reasons for Study Withdrawal		DR, SAC
5.	ITT	BL1	Listing of Subjects for Whom the Treatment Blind was Broken		DR, SAC
Protocol Deviations					
6.	ITT	DV2	Listing of Important Protocol Deviations		DR, SAC
7.	ASE	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations for Screen Failures		DR, SAC
8.	ITT	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		
Demographic and Baseline Characteristics					
9.	ITT	DM2	Listing of Demographic Characteristics		DR, SAC
10.	ITT	DM9	Listing of Race		DR, SAC
Prior and Concomitant Medications					
11.	ITT	CM3	Listing of Concomitant COPD Medications		DR, SAC
12.	ITT	CM3	Listing of Concomitant Non-COPD Medications		DR, SAC
Exposure					
13.	ITT	SAF_L01	Listing of Exposure Data		DR, SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Adverse Events					
14.	ASE	AE8	Listing of All Adverse Events		DR, SAC
15.	ASE	AE7	Listing of Subject Numbers for Individual Adverse Events		DR, SAC
Serious and Other Significant Adverse Events					
16.	ASE	AE8	Listing of Fatal Serious Adverse Events		DR, SAC
17.	ASE	AE8	Listing of Non-Fatal Serious Adverse Events		DR, SAC
18.	ASE	AE14	Listing of Reasons for Considering as a Serious Adverse Event		DR, SAC
19.	ASE	AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment		DR, SAC
20.	ITT	AE8	Listing of Adverse Events of Special Interest		DR, SAC
Vital signs					
21.	ITT	VS4	Listing of All Vital Signs Values		DR, SAC

10.9.11. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Study population					
22.	ASE	POP_L18	Listing of Unique Subject ID vs. Study Subject ID		DR, SAC
23.	ASE	POP_L03	Listing of Study Treatment Misallocations		DR, SAC
24.	ITT	POP_L04	Listing of Screening Lung Function, Reversibility Status, and GOLD Grade		DR, SAC
25.	ITT	POP_L05	Listing of Medical Conditions		DR, SAC
26.	ITT	POP_L06	Listing of Family History of Cardiovascular Risk Factors		DR, SAC
27.	ITT	POP_L07	Listing of COPD Duration and Exacerbation History		DR, SAC
28.	ITT	POP_L08	Listing of Smoking History and Smoking Status		DR, SAC
29.	ITT	POP_L09	Relationship between ATC Level 1, Ingredient, and Verbatim Text for Non-COPD Medications		DR, SAC
30.	ITT	POP_L10	Listing of Treatment Compliance Data	Including both run-in and on-treatment.	DR, SAC
Spirometry					
31.	ITT	EFF_L01	Listing of Raw FEV_1 (L) and FVC (L) Data		DR, SAC
COPD exacerbations					
32.	ITT	EFF_L02	Listing of COPD Exacerbations		DR, SAC
SGRQ					
33.	ITT	EFF_L03	Listing of SGRQ Scores	Include screening scores	DR, SAC
CAT					
34.	ITT	EFF_L04	Listing of CAT Scores	Include screening scores	DR, SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Adverse events					
35.	ITT	SAF_L02	Listing of AE Terms of Special Interest		DR, SAC
36.	ITT	AE7	Listing of Subject Numbers for On-Treatment Adverse Events of Special Interest		DR, SAC
Pneumonia incidence					
37.	ITT	SAF_L03	Listing of Pneumonia Data		DR, SAC
Bone fractures					
38.	ITT	SAF_L04	Listing of Bone Fracture Data		DR, SAC
Chest imaging (X-ray or CT scan)					
39.	ITT	SAF_L05	Listing of Chest Imaging (X-ray or CT scan) Data		DR, SAC
Liver events					
40.	ITT	SAF_L06	Listing of Liver Event Results and Time of Event Relative to Treatment		DR, SAC
41.	ITT	SAF_L07	Listing of Medical Conditions for Subjects with Liver Stopping Events		DR, SAC
42.	ITT	SAF_L08	Listing of Substance Use for Subjects with Liver Stopping Events		DR, SAC
43.	ITT	SAF_L09	Listing of Liver Event Information for RUCAM Scores		DR, SAC
44.	ITT	SAF_L10	Listing of Liver Biopsy Details		DR, SAC
45.	ITT	SAF_L11	Listing of Liver Imaging Details		DR, SAC
Inhaler malfunctions					
46.	ITT	SAF_L12	Listing of Inhaler Malfunctions		DR, SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Hepatitis B and C tests					
47.	ITT	SAF_L14	Listing of Hepatitis B and C Test Results	Hep B & C test results are included in datasets with lab data from vendor.	DR, SAC
ECG					
48.	ITT	SAF_L15	Listing of ECG Data		DR, SAC
Laboratory data					
49.	ITT	LB14	Listing of Laboratory Data with Character Results		DR, SAC

10.10. Appendix 10: Example Mock Shells for Data Displays

10.10.1. Tables

Example: POP_T01 Page 1 of x
Protocol: 207626
Population: All Subjects Enrolled

Table 1.1

Summary of Subject Populations and Reasons for Screen/Run-in Failure

Population	FF/UMEC/VI 100/62.5/25	TIO 18	Total
All subjects enrolled			xxx
Pre-screen failure			xxx (xxx%)
Attended screening visit			xxx (xxx%)
Screen failure [1]			xxx (xxx%)
Primary reason for screen failure [1]			
Did not meet inclusion/exclusion criteria			xxx (xxx%)
Serious adverse event			xxx (xxx%)
Investigator discretion			xxx (xxx%)
Withdrew consent			xxx (xxx%)
Unknown			xxx (xxx%)
Run-in failure			xxx
Primary reason for run-in failure [2]			
Serious adverse event			xxx (xxx%)
Protocol deviation			xxx (xxx%)

Study closed / terminated			xxx (xxx%)
Lost to follow-up			xxx (xxx%)
Investigator discretion			xxx (xxx%)
Withdrew consent			xxx (xxx%)
Did not meet continuation criteria			xxx (xxx%)
Randomized	xxx	xxx	xxx
Intent-to-Treat	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)

[1] Percentages are based on the number of subjects who attended the screening visit.
[2] Percentages are based on the number of subjects who were considered run-in failures.

<user ID: pathname datestamp timestamp>

Example: POP_T02 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Table 1.2
Summary of Attendance at Each Visit

Visit	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 N=xxx)	Total N=xxx)
Pre-Screening	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Screening / Run-in	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Day 1 (Randomization)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Day 28	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Day 84	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Day 85	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Follow-up	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)

Note: The pre-screening and screening visits may occur on the same day.

<user ID: pathname datestamp timestamp>

Example: POP_T03 Page 1 of 1
Protocol: 207626
Population: Intent-to-Treat

Table 1.10
Summary of Important Protocol Deviations

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Any important protocol deviations	xxx (xx%)	xxx (xx%)	xxx (xx%)
Informed consent	xx (xx%)	xx (xx%)	xx (xx%)
Eligibility criteria not met	xx (xx%)	xx (xx%)	xx (xx%)
Not withdrawn after developing withdrawal criteria	xx (xx%)	xx (xx%)	xx (xx%)
Excluded medication	xx (xx%)	xx (xx%)	xx (xx%)
Received incorrect treatment	xx (xx%)	xx (xx%)	xx (xx%)

Note: A subject may have more than one deviation.
<user ID: pathname datestamp timestamp>

Example: POP_T04
Protocol: 207626
Population: Intent-to-Treat

Table 1.17
Summary of Cardiovascular Risk Factors

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Any cardiovascular risk factor			
n	xxx	xxx	Xxx
Yes	xx (xx%)	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)	xx (xx%)
Number of cardiovascular risk factors			
n	xxx	xxx	Xxx
0	xx (xx%)	xx (xx%)	xx (xx%)
1	xx (xx%)	xx (xx%)	xx (xx%)
>=2	xx (xx%)	xx (xx%)	xx (xx%)

Note: Cardiovascular risk factors include past or current medical conditions recorded at screening.
<user ID: pathname datestamp timestamp>

Example: POP_T04
Protocol: 207626
Population: Intent-to-Treat

Table 1.17
Summary of Cardiovascular Risk Factors

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Cardiovascular risk factors			
Angina pectoris	xx (xx%)	xx (xx%)	xx (xx%)
Arrhythmia	xx (xx%)	xx (xx%)	xx (xx%)
Cerebrovascular accident	xx (xx%)	xx (xx%)	xx (xx%)
Congestive heart failure	xx (xx%)	xx (xx%)	xx (xx%)
Coronary artery disease	xx (xx%)	xx (xx%)	xx (xx%)
Diabetes mellitus	xx (xx%)	xx (xx%)	xx (xx%)
Hypercholesterolemia	xx (xx%)	xx (xx%)	xx (xx%)
Hypertension	xx (xx%)	xx (xx%)	xx (xx%)
Myocardial infarction	xx (xx%)	xx (xx%)	xx (xx%)

Note: Cardiovascular risk factors include past or current medical conditions recorded at screening.
<user ID: pathname datestamp timestamp>

Example: POP_T05
Protocol: 207626
Population: Intent-to-Treat

Table 1.18
Summary of Family History of Cardiovascular Risk Factors

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Family history of premature coronary artery disease (women <65 years old or men <55 years old)			
n	xxx	xxx	Xxx
Yes	xx (xx%)	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)	xx (xx%)
Family history of myocardial infarction			
n	xxx	xxx	Xxx
Yes	xx (xx%)	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)	xx (xx%)

Note: History in first-degree relatives only (biological parent, sibling, or offspring).

<user ID: pathname datestamp timestamp>

Example: POP_T05
Protocol: 207626
Population: Intent-to-Treat

Table 1.18
Summary of Family History of Cardiovascular Risk Factors

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Family history of stroke			
n	xxx	xxx	Xxx
Yes	xx (xx%)	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)	xx (xx%)

Note: History in first-degree relatives only (biological parent, sibling, or offspring).

<user ID: pathname datestamp timestamp>

Example: POP_T06
Protocol: 207626
Population: Intent-to-Treat

Table 1.19
Summary of Smoking History at Screening

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Average number of cigarettes smoked per day			
n	xxx	xxx	xxx
Mean	xx.x	xx.x	xx.x
SD	xx.xx	xx xx	xx.xx
Median	xx.x	xx.x	xx.x
Min.	x	x	x
Max.	xx	xx	xx
Number of years during which subject has smoked tobacco			
n	xxx	xxx	xxx
Mean	xx.x	xx.x	xx.x
SD	xx.xx	xx xx	xx.xx
Median	xx.x	xx.x	xx.x
Min.	x	x	x
Max.	xx	xx	xx

[1] Pack-years = (number of cigarettes smoked per day / 20) x number of years smoked
<user ID: pathname datestamp timestamp>

Table 1.19
Summary of Smoking History at Screening

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Number of pack-years [1]			
n	xxx	xxx	xxx
Mean	xx.x	xx.x	xx.x
SD	xx.xx	xx xx	xx.xx
Median	xx.x	xx.x	xx.x
Min.	x	x	x
Max.	xx	xx	xx

[1] Pack-years = (number of cigarettes smoked per day / 20) x number of years smoked

<user ID: pathname datestamp timestamp>

Example: POP_T07 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Table 1.20
Summary of Smoking Status at Screening

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
n	xx	xx	xx
Current smoker	xx (xx%)	xx (xx%)	xx (xx%)
Former smoker	xx (xx%)	xx (xx%)	xx (xx%)

<user ID: pathname datestamp timestamp>

Example: POP_T08 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Table 1.21
Summary of COPD History at Screening

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
COPD Type			
Chronic bronchitis	xx (xx%)	xx (xx%)	xx (xx%)
Emphysema	xx (xx%)	xx (xx%)	xx (xx%)
Chronic bronchitis and emphysema	xx (xx%)	xx (xx%)	xx (xx%)
COPD duration (years)			
n	xxx	xxx	xxx
<1 year	xx (xx%)	xx (xx%)	xx (xx%)
>=1 to <5 years	xx (xx%)	xx (xx%)	xx (xx%)
>=5 to <10 years	xx (xx%)	xx (xx%)	xx (xx%)
>=10 to <15 years	xx (xx%)	xx (xx%)	xx (xx%)
>=15 to <20 years	xx (xx%)	xx (xx%)	xx (xx%)
>=20 to <25 years	xx (xx%)	xx (xx%)	xx (xx%)
>=25 years	xx (xx%)	xx (xx%)	xx (xx%)

<user ID: pathname datestamp timestamp>

Example: POP_T09
Protocol: 207626
Population: Intent-to-Treat

Table 1.22
Summary of COPD Exacerbation History at Screening

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Number of exacerbations in the last 12 months that were managed without oral/systemic corticosteroids and/or antibiotics (not involving hospitalization)			
n	xxx	xxx	Xxx
0	xx (xx%)	xx (xx%)	xx (xx%)
1	xx (xx%)	xx (xx%)	xx (xx%)
>=2	xx (xx%)	xx (xx%)	xx (xx%)
Number of exacerbations in the last 12 months that required oral/systemic corticosteroids and/or antibiotics (not involving hospitalization)			
n	xxx	xxx	Xxx
0	xx (xx%)	xx (xx%)	xx (xx%)
1	xx (xx%)	xx (xx%)	xx (xx%)
>=2	xx (xx%)	xx (xx%)	xx (xx%)
Number of exacerbations in the last 12 months that required			

hospitalization			
n	xxx	xxx	Xxx
0	xx (xx%)	xx (xx%)	xx (xx%)
1	xx (xx%)	xx (xx%)	xx (xx%)
>=2	xx (xx%)	xx (xx%)	xx (xx%)
COPD Type			
Chronic bronchitis	xx (xx%)	xx (xx%)	xx (xx%)
Emphysema	xx (xx%)	xx (xx%)	xx (xx%)
Chronic bronchitis and emphysema	xx (xx%)	xx (xx%)	xx (xx%)

Note: Number of COPD exacerbations reported in the 12 months prior to the Screening Visit.
Note: Moderate exacerbations are defined as those that required treatment with oral/systemic corticosteroids and/or antibiotics (not involving hospitalisation). Severe exacerbations are defined as those that required in-patient hospitalisation.
<user ID: pathname datestamp timestamp>

Example: POP_T10
Protocol: 207626
Population: Intent-to-Treat

Table 1.23
Summary of Screening Lung Function

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Pre-bronchodilator FEV_1 (L)			
n	xxx	xxx	xxx
Mean	xx.xxx	xx.xxx	xx.xxx
SD	x.xxxx	x.xxxx	x.xxxx
Median	xx.xxx	xx.xxx	xx.xxx
Min.	xx.xx	xx.xx	xx.xx
Max.	xx.xx	xx.xx	xx.xx
Post-bronchodilator FEV_1 (L)			
n	xxx	xxx	xxx
Mean	xx.xxx	xx.xxx	xx.xxx
SD	x.xxxx	x.xxxx	x.xxxx
Median	xx.xxx	xx.xxx	xx.xxx
Min.	xx.xx	xx.xx	xx.xx
Max.	xx.xx	xx.xx	xx.xx

Programming note: Same format for Table 1.24 (Summary of Screening Lung Function by Country).

<user ID: pathname datestamp timestamp>

Table 1.23
Summary of Screening Lung Function

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Pre-bronchodilator FVC (L)			
n	xxx	xxx	xxx
Mean	xx.xxx	xx.xxx	xx.xxx
SD	x.xxxx	x.xxxx	x.xxxx
Median	xx.xxx	xx.xxx	xx.xxx
Min.	xx.xx	xx.xx	xx.xx
Max.	xx.xx	xx.xx	xx.xx
Post-bronchodilator FVC (L)			
n	xxx	xxx	xxx
Mean	xx.xxx	xx.xxx	xx.xxx
SD	x.xxxx	x.xxxx	x.xxxx
Median	xx.xxx	xx.xxx	xx.xxx
Min.	xx.xx	xx.xx	xx.xx
Max.	xx.xx	xx.xx	xx.xx

Programming note: Same format for Table 1.24 (Summary of Screening Lung Function by Country).

<user ID: pathname datestamp timestamp>

Table 1.23
Summary of Screening Lung Function

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Pre-bronchodilator FEV_1/FVC			
n	xxx	xxx	xxx
Mean	xx.xxx	xx.xxx	xx.xxx
SD	x.xxxx	x.xxxx	x.xxxx
Median	xx.xxx	xx.xxx	xx.xxx
Min.	xx.xx	xx.xx	xx.xx
Max.	xx.xx	xx.xx	xx.xx
Post-bronchodilator FEV_1/FVC			
n	xxx	xxx	xxx
Mean	xx.xxx	xx.xxx	xx.xxx
SD	x.xxxx	x.xxxx	x.xxxx
Median	xx.xxx	xx.xxx	xx.xxx
Min.	xx.xx	xx.xx	xx.xx
Max.	xx.xx	xx.xx	xx.xx

Programming note: Same format for Table 1.24 (Summary of Screening Lung Function by Country).

<user ID: pathname datestamp timestamp>

Table 1.23
Summary of Screening Lung Function

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Predicted FEV_1 (L)			
n	xxx	xxx	xxx
Mean	xx.xxx	xx.xxx	xx.xxx
SD	x.xxxx	x.xxxx	x.xxxx
Median	xx.xxx	xx.xxx	xx.xxx
Min.	xx.xx	xx.xx	xx.xx
Max.	xx.xx	xx.xx	xx.xx
Percent predicted FEV_1 (%)			
n	xxx	xxx	xxx
Mean	xx.xxx	xx.xxx	xx.xxx
SD	x.xxxx	x.xxxx	x.xxxx
Median	xx.xxx	xx.xxx	xx.xxx
Min.	xx.xx	xx.xx	xx.xx
Max.	xx.xx	xx.xx	xx.xx

Programming note: Same format for Table 1.24 (Summary of Screening Lung Function by Country).

<user ID: pathname datestamp timestamp>

Table 1.23
Summary of Screening Lung Function

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Reversibility (%)			
n	xxx	xxx	xxx
Mean	xx.xxx	xx.xxx	xx.xxx
SD	x.xxxx	x.xxxx	x.xxxx
Median	xx.xxx	xx.xxx	xx.xxx
Min.	xx.xx	xx.xx	xx.xx
Max.	xx.xx	xx.xx	xx.xx

Programming note: Same format for Table 1.24 (Summary of Screening Lung Function by Country).

<user ID: pathname datestamp timestamp>

Example: POP_T11
Protocol: 207626
Population: Intent-to-Treat

Table 1.25
Summary of Reversibility and GOLD Grade (1 – 4) at Screening

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Gold Grade			
n	xxx	xxx	Xxx
Grade 1 (mild): predicted FEV_1 >= 80%	xx (xx%)	xx (xx%)	xx (xx%)
Grade 2 (moderate): 50% <= predicted FEV_1 < 80%	xx (xx%)	xx (xx%)	xx (xx%)
Grade 3 (severe) 30% <= predicted FEV_1 < 50%	xx (xx%)	xx (xx%)	xx (xx%)
Grade 3 (very severe) predicted FEV_1 < 30%	xx (xx%)	xx (xx%)	xx (xx%)
Reversible to salbutamol [1]			
n	xxx	xxx	Xxx
Reversible	xx (xx%)	xx (xx%)	xx (xx%)
Not reversible	xx (xx%)	xx (xx%)	xx (xx%)
Exacerbation history in previous year			
N	xxx	xxx	Xxx
<2 moderate and no severe	xx (xx%)	xx (xx%)	xx (xx%)
>=2 moderate OR >=1 severe	xx (xx%)	xx (xx%)	xx (xx%)
GOLD grade / exacerbation history in previous year			
GOLD 1/2 with >=2 moderate or >=1 severe			
GOLD 3/4 with <2 moderate and no severe			
GOLD 3/4 with >=2 moderate or >=1 severe			

[1] "Reversible" is defined as an increase in FEV_1 of >=12% AND of >=200mL following administration of salbutamol. "Not reversible" is defined as an increase in FEV_1 of <200mL OR an increase of >=200mL that is <12% of the pre-salbutamol FEV_1.

Note: Moderate exacerbations are defined as exacerbations that required treatment with oral/systemic corticosteroids and/or antibiotics (not involving hospitalisation). Severe exacerbations are defined as exacerbations that required in-patient hospitalisation.

<user ID: pathname datestamp timestamp>

Example: POP_T11
Protocol: 207626
Population: Intent-to-Treat

Table 1.25
Summary of Reversibility and GOLD Grade (1 – 4) at Screening

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
GOLD grade / exacerbation history in previous year			
GOLD 1/2 with >=2 moderate or >=1 severe			
GOLD 3/4 with <2 moderate and no severe			
GOLD 3/4 with >=2 moderate or >=1 severe			

[1] "Reversible" is defined as an increase in FEV_1 of >=12% AND of >=200mL following administration of salbutamol. "Not reversible" is defined as an increase in FEV_1 of <200mL OR an increase of >=200mL that is <12% of the pre-salbutamol FEV_1.

Note: Moderate exacerbations are defined as exacerbations that required treatment with oral/systemic corticosteroids and/or antibiotics (not involving hospitalisation). Severe exacerbations are defined as exacerbations that required in-patient hospitalisation.

<user ID: pathname datestamp timestamp>

Example: POP_T12
Protocol: 207626
Population: Intent-to-Treat

Table 1.26
Summary of CAT Score and CAT Category at Screening

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
CAT score			
n	xxx	xxx	xxx
Mean	xx.x	xx.x	xx.x
SD	xx.xx	xx xx	xx.xx
Median	xx.x	xx.x	xx.x
Min.	x	x	x
Max.	xx	xx	xx
CAT category			
n	xxx	xxx	Xxx
CAT < 10	xx (xx%)	xx (xx%)	xx (xx%)
CAT >= 10	xx (xx%)	xx (xx%)	xx (xx%)

<user ID: pathname datestamp timestamp>

Example: POP_T13
Protocol: 207626
Population: Intent-to-Treat

Table 1.27
Summary of COPD Concomitant Medications Taken Prior to Screening

Respiratory Class Ingredient	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
Any medication	xxx (xx%)	xxx (xx%)	xxx (xx%)
xxxxxxxxxxxxxx			
Any medication	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxx + xxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxxxxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxx + xxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxxx + xxxxxxxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxxxxxxxxxxxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxx + xxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxxxxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxx + xxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxxx + xxxxxxxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxxxxxxxxxxxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxxxxxxxxxx			
Any medication	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxx + xxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxxxxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxxx + xxxxxxxxxx	xx (xx%)	xx (xx%)	xxx (xx%)
xxxxxxxxx	xx (xx%)	xx (xx%)	xxx (xx%)

Programming not: same format for Table 1.29 (Summary of COPD Concomitant Medications Taken during Run-in for Reasons other than an Exacerbation) and Table 1.32 (Summary of COPD Concomitant Medications Taken during Run-in for an Exacerbation).

Note: Combination products are included in all applicable respiratory classes.
Note: Study provided salbutamol was not recorded as a concomitant medication.
<user ID: pathname datestamp timestamp>

Example: POP_T14
Protocol: 207626
Population: Intent-to-Treat

Table 1.28
Summary of COPD Concomitant Medication Combinations Taken Prior to Screening

Medication Combination [1] Full Medication Combination [2]	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
None	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)
xxx + xxx + xxx + xxx	xx (xx%)	xx (xx%)	xx (xx%)

[1] COPD respiratory medication class (RMC) combination based on the individual RMC and any combination of the RMCs: ICS, LABA, LAMA, Xanthine and PDE4 Inhibitors.
[2] COPD RMC combination based on all RMCs.

<user ID: pathname datestamp timestamp>

Example: POP_T15
Protocol: 207626
Population: Intent-to-Treat

Table 1.30
Summary of On-Treatment COPD Concomitant Medications Taken for Reasons other than an Exacerbation

Respiratory Class Ingredient	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Any medication	xxx (xx%)	xxx (xx%)
xxxxxxxxxxxxxx		
Any medication	xx (xx%)	xx (xx%)
xxxxxx + xxxxx	xx (xx%)	xx (xx%)
xxxxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxx + xxxxx	xx (xx%)	xx (xx%)
xxxxxxxx + xxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxxxxxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxx + xxxxx	xx (xx%)	xx (xx%)
xxxxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxx + xxxxx	xx (xx%)	xx (xx%)
xxxxxxxx + xxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxxxxxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxxxxx		
Any medication	xx (xx%)	xx (xx%)
xxxxxx + xxxxx	xx (xx%)	xx (xx%)
xxxxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxx + xxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxxx	xx (xx%)	xx (xx%)

Programming note: Same format for Table 1.31 (Summary of Post-Treatment COPD Concomitant Medications Taken for Reasons other than an Exacerbation), Table 1.33 (Summary of On-Treatment COPD Concomitant Medications Taken for an Exacerbation), and Table 1.34 (Summary of Post-Treatment COPD Concomitant Medications Taken for an Exacerbation),

Note: Combination products are included in all applicable respiratory classes.
Note: Study provided salbutamol was not recorded as a concomitant medication.
Note: On-treatment medications include medications stopped on the day of randomization.
<user ID: pathname datestamp timestamp>

Example: POP_T16
Protocol: 207626
Population: Intent-to-Treat

Table 1.35
Summary of On-Treatment Non-COPD Concomitant Medications

ATC Level 1 Ingredient	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Any medication	xxx (xx%)	xxx (xx%)
xxxxxxxxxxxxxx		
Any medication	xx (xx%)	xx (xx%)
xxxxxx + xxxxx	xx (xx%)	xx (xx%)
xxxxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxx + xxxxx	xx (xx%)	xx (xx%)
xxxxxxxx + xxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxxxxxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxx + xxxxx	xx (xx%)	xx (xx%)
xxxxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxx + xxxxx	xx (xx%)	xx (xx%)
xxxxxxxx + xxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxxxxxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxxxxx		
Any medication	xx (xx%)	xx (xx%)
xxxxxx + xxxxx	xx (xx%)	xx (xx%)
xxxxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxx + xxxxxxxxxx	xx (xx%)	xx (xx%)
xxxxxxxxx	xx (xx%)	xx (xx%)

Programming note: Same format for Table 1.36 (Summary of Post-Treatment Non-COPD Concomitant Medications).

Note: Combination products are included in all applicable ATC level 1 categories.
Note: On-treatment medications include medications stopped on the day of randomization.

<user ID: pathname datestamp timestamp>

<user ID: pathname datestamp timestamp>

Example: POP_T17 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Table 1.37
Summary of Treatment Compliance

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)	Total (N=xxx)
ELLIPTA compliance (%)			
n	xxx	xxx	xxx
Mean	xx.x	xx.x	xx.x
SD	x.xx	x.xx	x.xx
Median	xx.x	xx.x	xx.x
Min.	xx.x	xx.x	xx.x
Max.	xx.x	xx.x	xx.x
<80%	xx (xx%)	xx (xx%)	xx (xx%)
>=80% to <95%	xx (xx%)	xx (xx%)	xx (xx%)
>=95% to <=105%	xx (xx%)	xx (xx%)	xx (xx%)
>105% to <=120%	xx (xx%)	xx (xx%)	xx (xx%)
>120%	xx (xx%)	xx (xx%)	xx (xx%)

Programming note: repeat this section for HANDIHALER compliance (%) and Overall compliance (%).

Note: High compliance values may be due to the imputation in the denominator of missing treatment stop dates with the date study treatment was last known to be taken.

<user ID: pathname datestamp timestamp>

Example: EFF_T01
Protocol: 207626
Population: Intent-to-Treat

Table 2.1
Summary of Baseline FEV_1 (L)

		FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
All subjects	n	xxx	xxx
	Mean	xx.xxx	xx.xxx
	SD	x.xxxx	x.xxxx
	Min.	xx.xx	xx.xx
	Q1	xx.xxx	xx.xxx
	Median	xx.xxx	xx.xxx
	Q3	xx.xxx	xx.xxx
	Max.	xx.xx	xx.xx
Subjects with non-missing on-treatment trough FEV_1 data at Day 85	n	xxx	xxx
	Mean	xx.xxx	xx.xxx
	SD	x.xxxx	x.xxxx
	Min.	xx.xx	xx.xx
	Q1	xx.xxx	xx.xxx
	Median	xx.xxx	xx.xxx
	Q3	xx.xxx	xx.xxx
	Max.	xx.xx	xx.xx
Subjects with missing			

on-treatment trough FEV_1 data at Day 85	n	xxx	xxx
	Mean	xx.xxx	xx.xxx
	SD	x.xxxx	x.xxxx
	Min.	xx.xx	xx.xx
	Q1	xx.xxx	xx.xxx
	Median	xx.xxx	xx.xxx
	Q3	xx.xxx	xx.xxx
	Max.	xx.xx	xx.xx

Programming note: Same format for Table 2.2 (Summary of Baseline FEV_1 (L) by Country).

Note: Baseline is the average of the two pre-dose measurements on Day 1.

<user ID: pathname datestamp timestamp>

Example: EFF_T02 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Table 2.3
Summary of Trough FEV_1 (L) - Hypothetical Estimand

			FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Day 28	Trough FEV1 (L)	n	xxx	xxx
		Mean	x.xxx	x.xxx
		SD	x.xxxx	x.xxxx
		Min.	x.xx	x.xx
		Q1	x.xxx	x.xxx
		Median	x.xxx	x.xxx
		Q3	x.xxx	x.xxx
		Max.	x.xx	x.xx
	Change from baseline	n	xxx	xxx
		Mean	x.xxx	x.xxx
		SD	x.xxxx	x.xxxx
		Min.	x.xx	x.xx
		Q1	x.xxx	x.xxx
		Median	x.xxx	x.xxx
		Q3	x.xxx	x.xxx
		Max.	x.xx	x.xx
Day 84	Trough FEV1 (L)	n	xxx	xxx
		Mean	x.xxx	x.xxx
		SD	x.xxxx	x.xxxx
		Min.	x.xx	x.xx
		Q1	x.xxx	x.xxx
		Median	x.xxx	x.xxx
		Q3	x.xxx	x.xxx

	Max.	x.xx	x.xx
Change from baseline	n	xxx	xxx
	Mean	x.xxx	x.xxx
	SD	x.xxxx	x.xxxx
	Min.	x.xx	x.xx
	Q1	x.xxx	x.xxx
	Median	x.xxx	x.xxx
	Q3	x.xxx	x.xxx
	Max.	x.xx	x.xx

<user ID: pathname datestamp timestamp>

Example: EFF_T02
Protocol: 207626
Population: Intent-to-Treat

Table 2.3
Summary of Trough FEV_1 (L) - Hypothetical Estimand

			FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Day 85	Trough FEV1 (L)	n	xxx	xxx
		Mean	x.xxx	x.xxx
		SD	x.xxxx	x.xxxx
		Min.	x.xx	x.xx
		Q1	x.xxx	x.xxx
		Median	x.xxx	x.xxx
		Q3	x.xxx	x.xxx
		Max.	x.xx	x.xx
	Change from baseline	n	xxx	xxx
		Mean	x.xxx	x.xxx
		SD	x.xxxx	x.xxxx
		Min.	x.xx	x.xx
		Q1	x.xxx	x.xxx
		Median	x.xxx	x.xxx
		Q3	x.xxx	x.xxx
		Max.	x.xx	x.xx

Programming note: Same format for Table 2.4 (Summary of Trough FEV_1– Treatment Policy Estimand), Table 2.5 (Summary of Trough FEV_1 by Country – Hypothetical Estimand), and Table 2.6 (Summary of Trough FEV_1 by Country – Treatment Policy Estimand).

Programming note: Same format for Table 2.12 (Summary of SGRQ Total and Domain Scores – Hypothetical Estimand), but will include total score and 3 domain scores (Symptoms, Activity, and Impacts) on Days 28 and 84.

Programming note: Same format for Table 2.17(Summary of CAT Score – Hypothetical Estimand) on Days 28 and 84.

<user ID: pathname datestamp timestamp>

Example: EFF_T03
Protocol: 207626
Population: Intent-to-Treat

Table 2.7
Analysis of Trough FEV_1 (L) – Hypothetical Estimand

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Day 28		
n	Xxx	xxx
LS mean (SE)	x.xxx (x.xxxx)	x.xxx (x.xxxx)
95% CI	(x.xxx, x.xxx)	(x.xxx, x.xxx)
LS mean change (SE)	x.xxx (x.xxxx)	x.xxx (x.xxxx)
95% CI	(x.xxx, x.xxx)	(x.xxx, x.xxx)
FF/UMEC/VI 100/62.5/25 VS TIO 18		
Difference (SE)	x.xxx (x.xxxx)	
95% CI	(x.xxx, x.xxx)	
p-value	x.xxx	
Day 84		
n	Xxx	xxx
LS mean (SE)	x.xxx (x.xxxx)	x.xxx (x.xxxx)
95% CI	(x.xxx, x.xxx)	(x.xxx, x.xxx)
LS mean change (SE)	x.xxx (x.xxxx)	x.xxx (x.xxxx)
95% CI	(x.xxx, x.xxx)	(x.xxx, x.xxx)
FF/UMEC/VI 100/62.5/25 VS TIO 18		
Difference (SE)	x.xxx (x.xxxx)	
95% CI	(x.xxx, x.xxx)	
p-value	x.xxx	

Note: Analysis consists of a repeated measures model with covariates of baseline value, visit, geographical region, treatment, and interactions of visit with treatment and baseline value.

Programming note: Same format for Table 2.8 (Analysis of Trough FEV_1 – Treatment Policy Estimand).

Programming note: Same format for Table 2.13 (Analysis of SGRQ Total Score – Hypothetical Estimand) on Days 28 and 84 only.

Programming note: Same format for Table 2.21 (Analysis of CAT Score – Hypothetical Estimand) on Days 28 and 84 only.

<user ID: pathname datestamp timestamp>

Example: EFF_T03
Protocol: 207626
Population: Intent-to-Treat

Table 2.7
Analysis of Trough FEV_1 (L) – Hypothetical Estimand

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Day 85		
n	xxx	xxx
LS mean (SE)	x.xxx (x.xxxx)	x.xxx (x.xxxx)
95% CI	(x.xxx, x.xxx)	(x.xxx, x.xxx)
LS mean change (SE)	x.xxx (x.xxxx)	x.xxx (x.xxxx)
95% CI	(x.xxx, x.xxx)	(x.xxx, x.xxx)
FF/UMEC/VI 100/62.5/25 VS TIO 18		
Difference (SE)	x.xxx (x.xxxx)	
95% CI	(x.xxx, x.xxx)	
p-value	x.xxx	

Note: Analysis consists of a repeated measures model with covariates of baseline value, visit, geographical region, treatment, and interactions of visit by treatment and visit by baseline.

Programming note: Same format for Table 2.8 (Analysis of Trough FEV_1 – Treatment Policy Estimand).

Programming note: Same format for Table 2.13 (Analysis of SGRQ Total Score – Hypothetical Estimand) on Days 28 and 84 only.

Programming note: Same format for Table 2.21 (Analysis of CAT Score – Hypothetical Estimand) on Days 28 and 84 only.

<user ID: pathname datestamp timestamp>

Example: EFF_T04 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Table 2.9
Significance Level for Interaction of Treatment with Geographical Region and Baseline FEV_1 for Analysis of Trough FEV_1 (L)on Day 85 – Treatment Policy Estimand

Interaction of treatment with:	p-value [1]
Baseline FEV1	x.xxx
Geographical region	x.xxx

[1] Analysis consists of a repeated measures model with covariates of baseline value, visit, geographical region, and treatment, as well as visit by treatment and visit by baseline interaction.

Note: An interaction is considered statistically significant if the p-value is <0.10.

Programming note: Same format for Table 2.10 (Significance Level for Interaction of Treatment with Geographical Region and Baseline FEV_1 for Analysis of Trough FEV_1 (L)on Day 85 – Hypothetical Estimand)
<user ID: pathname datestamp timestamp>

Example: EFF_T05 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Table 2.11
Tipping Point Sensitivity Analysis: Two-Sided p-values after Imputing Various Day 85 Mean Changes from Baseline Trough FEV_1 (L) – Treatment Policy Estimand

TIO 18	FF/UMEC/VI 100/62.5/25						
	-0.15	-0.10	-0.05	0.00	0.05	0.10	0.15
-0.15	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
-0.10	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
-0.05	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
0.00	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
0.05	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
0.10	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
0.15	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx

Note: Each column and each row represents a step-wise increment in the magnitude of the change from baseline in trough FEV_1.
Note: Data for subjects with missing baseline values were not imputed.
Note: Multiple imputation at Day 85 followed by Day 28 and Day 84 was calculated for all subjects with a missing on-treatment assessment, adjusting for covariates of geographical region and treatment. Imputed values were taken from a multivariate normal distribution with the assumed mean change from baseline and standard deviation taken from observed data at the corresponding time point.
Note: Analysis, including observed and imputed data at Day 85, used an ANCOVA model with covariates of baseline value, geographical region, and treatment.

*Programming note: Add * before each p-value that is less than 0.050.*
<user ID: pathname datestamp timestamp>

Example: EFF_T06
Protocol: 207626
Population: Intent-to-Treat

Table 2.12
Summary of Baseline SGRQ Total and Domain Scores

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
SGRQ total score		
N	xxx	xxx
Mean	xx.x	xx.x
SD	xx.xx	xx.xx
Min.	x	x
Q1	xx.x	xx.x
Median	xx.x	xx.x
Q3	xx.x	xx.x
Max.	xx	xx
Symptoms domain		
N	xxx	xxx
Mean	xx.x	xx.x
SD	xx.xx	xx xx
Min.	x	x
Q1	xx.x	xx.x
Median	xx.x	xx.x
Q3	xx.x	xx.x
Max.	xx	xx

Programming note: Same format for Table 2.19 (Summary of Baseline CAT Score).

<user ID: pathname datestamp timestamp>

Example: EFF_T06
Protocol: 207626
Population: Intent-to-Treat

Table 2.12
Summary of Baseline SGRQ Total and Domain Scores

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Activity domain		
N	xxx	xxx
Mean	xx.x	xx.x
SD	xx.xx	xx xx
Min.	x	x
Q1	xx.x	xx.x
Median	xx.x	xx.x
Q3	xx.x	xx.x
Max.	xx	xx
Impacts domain		
N	xxx	xxx
Mean	xx.x	xx.x
SD	xx.xx	xx xx
Min.	x	x
Q1	xx.x	xx.x
Median	xx.x	xx.x
Q3	xx.x	xx.x
Max.	xx	xx

Programming note: Same format for Table 2.19 (Summary of Baseline CAT Score).

<user ID: pathname datestamp timestamp>

Example: EFF_T03
Protocol: 207626
Population: Intent-to-Treat

Table 2.14

Analysis of SGRQ Total Score – Hypothetical Estimand

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Day 28		
n [1]	xxx	xxx
n [2]	xxx	xxx
LS Mean (SE)	x.x (x.xx)	x.x (x.xx)
95% CI	(x.x, x.x)	(x.x, x.x)
LS Mean Change (SE)	x.x (x.xx)	x.x (x.xx)
95% CI	(x.x, x.x)	(x.x, x.x)
FF/UMEC/VI 100/62.5/25 VS TIO 18		
Difference (SE)	x.x (x.xx)	
95% CI	(x.x, x.x)	
p-value	x.xxx	

[1] Number of subjects with analyzable data for one or more time points.
[2] Number of subjects with analyzable data at the current time point.
Note: Analysis performed using a repeated measures model with covariates of baseline value, visit, geographical region, treatment, visit by treatment and visit by baseline interactions.
<user ID: pathname datestamp timestamp>

Example: EFF_T03
Protocol: 207626
Population: Intent-to-Treat

Table 2.14
Analysis of SGRQ Total Score – Hypothetical Estimand

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Day 84		
n [1]	xxx	xxx
n [2]	xxx	xxx
LS Mean (SE)	x.x (x.xx)	x.x (x.xx)
95% CI	(x.x, x.x)	(x.x, x.x)
LS Mean Change (SE)	x.x (x.xx)	x.x (x.xx)
95% CI	(x.x, x.x)	(x.x, x.x)
FF/UMEC/VI 100/62.5/25 VS TIO 18		
Difference (SE)	x.x (x.xx)	
95% CI	(x.x, x.x)	
p-value	x.xxx	

[1] Number of subjects with analyzable data for one or more time points.
[2] Number of subjects with analyzable data at the current time point.
Note: Analysis performed using a repeated measures model with covariates of baseline value, visit, geographical region, treatment, visit by treatment and visit by baseline interactions.
<user ID: pathname datestamp timestamp>

Example: EFF_T07 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Table 2.15
Summary and Analysis of Proportion of Responders as Defined by SGRQ Total Score – Hypothetical Estimand

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Day 28		
n	xxx	xxx
Responders	xxx (xx%)	xxx (xx%)
Non-responders	xxx (xx%)	xxx (xx%)
FF/UMEC/VI 100/62.5/25 VS TIO 18		
Odds ratio	x.xx	
95% CI	(x.xx, x.xx)	
p-value	x.xxx	
Day 84		
n	xxx	xxx
Responders	xxx (xx%)	xxx (xx%)
Non-responders	xxx (xx%)	xxx (xx%)
FF/UMEC/VI 100/62.5/25 VS TIO 18		
Odds ratio	x.xx	
95% CI	(x.xx, x.xx)	
p-value	x.xxx	

Note: Responders are defined as those subjects whose SGRQ total score is 4 units or more below baseline. Non-responders are defined as those subjects whose SGRQ total score is more than 4 units below baseline or a missing SGRQ total score at a the timepoint in question and no subsequent on-treatment scores. Subjects will not be assigned a responder status at any timepoint if their baseline SGRQ total score is missing. Subjects will not have a responder status assigned at a given timepoint if the SGRQ total score at that timepoint is missing.

Note: Analysis is based on a generalized linear mixed model with a logit link function and covariates of treatment group, visit, geographical region, baseline SGRQ score, and interactions of visit with baseline SGRQ score and with treatment.

Programming note: same format and same timepoints for Table 2.23 (Summary and Analysis of Proportion of Responders as Defined by CAT Score – Hypothetical Estimand). Highlighted text in footnote above should be changed as follows:

SGRQ total score is 4 units => CAT score is 2 units

SGRQ total score is more than 4 units => CAT score is more than 2 units

SGRQ total score => CAT score

<user ID: pathname datestamp timestamp>

Example: EFF_T08
Protocol: 207626
Population: Intent-to-Treat

Table 2.16
Summary of On-Treatment COPD Exacerbations

	FF/UMEC/VI 100/62.5/25 (N=xxx)		TIO 18 (N=xxx)	
	n (%)	Rate (#)	n (%)	Rate (%)
Total treatment exposure (subject-years)		xxx.x		xxx.x
Subjects with a mild, moderate, or severe COPD exacerbation	xxx (xx)	xxx.x (xx)	xxx (xx)	xxx.x (xx)
Subjects with a mild COPD exacerbation	xxx (xx)	xxx.x (xx	xxx (xx)	xxx.x (xx)
Subjects with a moderate COPD exacerbation	xxx (xx)	xxx.x (xx	xxx (xx)	xxx.x (xx)
Subjects with a severe COPD exacerbation	xxx (xx)	xxx.x (xx	xxx (xx)	xxx.x (xx)
Subjects with a moderate/severe COPD exacerbation	xxx (xx)	xxx.x (xx	xxx (xx)	xxx.x (xx)
Total number of moderate/severe COPD exacerbations per subject				
n		xxx (xx)		xxx (xx)
0		xxx (xx)		xxx (xx)
1		xxx (xx)		xxx (xx)
2		xxx (xx)		xxx (xx)
>=3		xxx (xx)		xxx (xx)
Subjects with >=2 moderate/severe COPD exacerbations		xxx (xx)		xxx (xx)

Note: n = number of subjects, # = number of COPD exacerbations.
Note: Rate is the event rate per 1000 subject-years, calculated as the number of events x 1000, divided by the total duration at risk.
Note: Moderate exacerbations are defined as those that required treatment with oral or systemic corticosteroids and/or antibiotics (not involving hospitalizations or resulting in death). Severe exacerbations are defined as those that required hospitalization or resulted in death.

Programming note: Same format for Table 2.18 (Summary of Post-treatment COPD Exacerbations).

<user ID: pathname datestamp timestamp>

Example: EFF_T09
Protocol: 207626
Population: Intent-to-Treat

Table 2.17
Summary of On-Treatment Details of COPD Exacerbations

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Total number of moderate/severe COPD exacerbations	xxxx	xxxx
Treatment [1]		
Oral/systemic corticosteroids	xxx (xx)	xxx (xx)
Antibiotics	xxx (xx)	xxx (xx)
Emergency room visit	xxx (xx)	xxx (xx)
Hospitalization	xxx (xx)	xxx (xx)
Severity of Exacerbation		
Mild	xxx (xx)	xxx (xx)
Moderate	xxx (xx)	xxx (xx)
Severe	xxx (xx)	xxx (xx)
Outcome		
Resolved	xxx (xx)	xxx (xx)
Fatal	xxx (xx)	xxx (xx)
Not resolved	xxx (xx)	xxx (xx)

[1] More than one treatment could have been recorded for a given exacerbation.

Note: Percentages are calculated using the total number of moderate/severe COPD exacerbations as the denominator.
Note: Rate is the event rate per 1000 subject-years, calculated as the number of events x 1000, divided by the total treatment exposure through Day 85.

Programming note: Same format for Table 2.19 (Summary of Post-Treatment Details of COPD Exacerbations).

<user ID: pathname datestamp timestamp>

Example: EFF_T09
Protocol: 207626
Population: Intent-to-Treat

Table 2.17
Summary of On-Treatment Details of COPD Exacerbations

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Duration of exacerbation (days)		
n	xxx	xxx
Mean	xx.x	xx.x
SD	xx.xx	xx xx
Median	xx.x	xx.x
Min.	x	x
Max.	xx	xx

[1] Percentages are calculated using the number of exacerbations of any severity as the denominator.
[2] More than one treatment could have been recorded for a given exacerbation.
Note: Rate is the event rate per 1000 subject-years, calculated as the number of events x 1000, divided by the total treatment exposure through Day 85.

Programming note: Same format for Table 2.19 (Summary of Post-Treatment COPD Exacerbation Details). The description for the first row in the table should be 'Total time in study post-treatment (subject-years'.

<user ID: pathname datestamp timestamp>

Example: SAF_T01
Protocol: 207626
Population: Intent-to-Treat

Table 3.1
Summary of Exposure

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Exposure (days)		
n	xxx	xxx
Mean	xx.x	xx.x
SD	xx.xx	xx.xx
Median	xx.x	xx.xx
Min.	xx	xx
Max.	xxx	xxx
Total treatment exposure (subject-years)	xxx.x	xxx.x
Duration of exposure		
>=1 day	xx (xx%)	xx (xx%)
>=4 weeks	xx (xx%)	xx (xx%)
>=8 weeks	xx (xx%)	xx (xx%)
>=12 weeks	xx (xx%)	xx (xx%)
11-13 weeks	xx (xx%)	xx (xx%)
Total time in study post-treatment (subject-years)	xxx.x	xxx.x

<user ID: pathname datestamp timestamp>

Example: SAF_T02 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Table 3.23
Summary of On-Treatment Pneumonia Incidence

	FF/UMEC/VI 100/62.5/25 (N=xxx)		TIO 18 (N=xxx)	
	n (%)	Rate (%)	n (%)	Rate (%)
Total treatment exposure (subject-years)		xxx.x		xxx.x
Subjects with pneumonia	xxx (xx)	xxx.x (xx)	xxx (xx)	xxx.x (xx)
Subjects with pneumonia supported by X-ray or CT scan	xxx (xx)	xxx.x (xx)	xxx (xx)	xxx.x (xx)
Total number (%) of pneumonia cases per subject				
n		xxx (xx)		xxx (xx)
0		xxx (xx)		xxx (xx)
1		xxx (xx)		xxx (xx)
>=2		xxx (xx)		xxx (xx)

Note: n=Number of subjects, #=Number of events.
Note: Rate is event rate per 1000 subject-years, calculated as the number of events x 1000, divided by the total treatment exposure.
Note: A chest x-ray/CT scan is associated with pneumonia if it is taken during the pneumonia or within -7 to +10 days (inclusive) of the date of onset.
Note: Pneumonia is supported by a chest x-ray/CT scan if there is an associated x-ray/CT scan which shows the presence of infiltrates.
Note: Summary includes only pneumonia events reported on the pneumonia eCRF page.

Programming note: Same format for Table 3.25 (Summary of Post-Treatment Pneumonia Incidence).

<user ID: pathname datestamp timestamp>

Example: SAF_T03
Protocol: 207626
Population: Intent-to-Treat

Table 3.26

Summary of On-Treatment Details of Pneumonia

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Total number of cases of pneumonia	xx	xx
Cases of pneumonia with onset at most 14 days after the start of a moderate/severe exacerbation	xx (xx%)	xx (xx%)
Chest x-ray/CT scan taken	xx (xx%)	xx (xx%)
Findings consistent with diagnosis of pneumonia	xx (xx%)	xx (xx%)
No chest x-ray/CT scan taken	xx (xx%)	xx (xx%)
Hospitalised	xx (xx%)	xx (xx%)
Hospitalised and chest x-ray/CT scan taken	xx (xx%)	xx (xx%)
Findings consistent with diagnosis of pneumonia	x (xx%)	x (xx%)
No chest x-ray/CT scan taken	x (xx%)	x (xx%)
Fatal	xx (xx%)	xx (xx%)
Fatal and chest x-ray/CT scan taken	xx (xx%)	xx (xx%)
Findings consistent with diagnosis of pneumonia	xx (xx%)	xx (xx%)
No chest x-ray/CT scan taken	xx (xx%)	xx (xx%)

Note: Table summarizes event counts. Percentages are calculated using the number of cases of pneumonia as the denominator.
Note: A chest x-ray/CT scan is associated with pneumonia if it is taken within the duration of the pneumonia or within -7 to +10 days (inclusive) of the date of onset.
Note: Summary includes pneumonia events reported on the pneumonia eCRF page.
<user ID: pathname datestamp timestamp>

Example: SAF_T03
Protocol: 207626
Population: Intent-to-Treat

Table 3.25
Summary of On-Treatment Details of Pneumonia

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Level of cough		
Increased level	xx (xx%)	xx (xx%)
Usual level	xx (xx%)	xx (xx%)
Increased sputum purulence		
Yes	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)
Lung evaluation shows crackles/rales, bronchial or bronchovesicular breath sounds		
Yes	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)
Worsening dypsnea		
Yes	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)

Note: Table summarizes event counts. Percentages are calculated using the number of cases of pneumonia as the denominator.
Note: A chest x-ray/CT scan is associated with pneumonia if it is taken within the duration of the pneumonia or within -7 to +10 days (inclusive) of the date of onset.
Note: Summary includes pneumonia events reported on the pneumonia eCRF page.

<user ID: pathname datestamp timestamp>

Example: SAF_T03
Protocol: 207626
Population: Intent-to-Treat

Table 3.25
Summary of On-Treatment Details of Pneumonia

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Does subject have pleural effusion?		
Yes	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)
Does subject have hypoxemia?		
Yes	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)
WBC count performed at time of event		
Yes	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)
WBC count relative to reference range		
High WBC	xx (xx%)	xx (xx%)
Normal WBC	xx (xx%)	xx (xx%)
Low WBC	xx (xx%)	xx (xx%)

Note: Table summarizes event counts. Percentages are calculated using the number of cases of pneumonia as the denominator.
Note: A chest x-ray/CT scan is associated with pneumonia if it is taken within the duration of the pneumonia or within -7 to +10 days (inclusive) of the date of onset.
Note: Summary includes pneumonia events reported on the pneumonia eCRF page.
<user ID: pathname datestamp timestamp>

Example: SAF_T03
Protocol: 207626
Population: Intent-to-Treat

Table 3.25
Summary of On-Treatment Details of Pneumonia

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Was BUN >19mg/dL (7mmol/L)?		
Yes	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)
Was there evidence the subject was confused?		
Yes	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)
Was the subject in an inpatient healthcare setting when the pneumonia developed?		
Yes	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)
Was a culture/swab taken?		
Yes	xx (xx%)	xx (xx%)
No	xx (xx%)	xx (xx%)
Unknown	xx (xx%)	xx (xx%)

Note: Table summarizes event counts. Percentages are calculated using the number of cases of pneumonia as the denominator.
Note: A chest x-ray/CT scan is associated with pneumonia if it is taken within the duration of the pneumonia or within -7 to +10 days (inclusive) of the date of onset.
Note: Summary includes pneumonia events reported on the pneumonia eCRF page.

<user ID: pathname datestamp timestamp>
Programming note: Same format for Table 3.26 (Summary of Post-Treatment Details of Pneumonia).

Example: SAF_T04 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Table 3.27
Summary of On-Treatment Bone Fractures

	FF/UMEC/VI 100/62.5/25 (N=xxx)		TIO 18 (N=xxx)	
	n (%)	Rate (%)	n (%)	Rate (%)
Total treatment exposure (subject-years)_		xxx.x		xxx.x
Subjects with at least one bone fracture incident	xxx (xx)	xxx.x (xx)	xxx (xx)	xxx.x (xx)
Total number (%) of bone fracture incidents per subject				
n		xxx (xx)		xxx (xx)
0		xxx (xx)		xxx (xx)
1		xxx (xx)		xxx (xx)
>=2		xxx (xx)		xxx (xx)
Number of fracture incidents which were [1]:				
Non-traumatic		xxx (xx)		xxx (xx)
Traumatic		xxx (xx)		xxx (xx)
Subjects with at least one bone fracture	xxx (xx)	xxx.x (xx)	xxx (xx)	xxx.x (xx)
Fracture location [2, 3]				
Chest		xxx (xx)		xxx (xx)
Ankle joint		xxx (xx)		xxx (xx)

Arm	xxx (xx)	xxx (xx)
Foot	xxx (xx)	xxx (xx)
Thoracic vertebra	xxx (xx)	xxx (xx)

[1] Percentages calculated using the number of bone fracture incidents as the denominator.
[2] Percentages calculated using the number of bone fractures as the denominator.
[3] Fracture locations are only displayed when there is at least one fracture in either treatment group.
Note: n = Number of subjects, # = Number of fracture incidents.
Note: Rate is event rate per 1000 subject-years, calculated as the number of fracture incidents x 1000, divided by the total treatment exposure.
Note: Fractures in multiple locations with the same date of fracture are considered to comprise one fracture incident.

Programming note: Same format for Table 3.28 (Summary of Post-Treatment Bone Fractures).

<user ID: pathname datestamp timestamp>

Example: SAF_T05
Protocol: 207626
Population: Intent-to-Treat

Table 3.29
Summary of Chest Imaging (X-Ray or CT Scan)

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Total number chest x-rays/CT scans taken:		
Associated with pneumonia	xxx (xx)	xxx (xx)
Associated with moderate/severe exacerbation	xxx (xx)	xxx (xx)
Findings consistent with diagnosis of pneumonia	xxx (xx)	xxx (xx)

Note: A chest x-ray/CT scan is associated with pneumonia if it is taken during the pneumonia or within -7 to +10 days (inclusive) of the date of onset.
Note: A chest x-ray/CT scan is associated with an exacerbation if it is taken during the exacerbation or within -7 to +10 days (inclusive) of the date of onset
Note: A single x-ray/CT scan can be associated with both pneumonia and an exacerbation.
Note: Summary includes on- and post-treatment chest x-rays/CT scans which were associated with an on-treatment case of pneumonia and/or exacerbation.
Note: Percentages are based on the total number of assessments/events within each summary.

<user ID: pathname datestamp timestamp>

Example: SAF_T06
Protocol: 207626
Population: Intent-to-Treat

Table 3.30
Summary of Blood Chemistry Results at Screening

Lab test	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
Albumin (g/L)		
n	xxx	xxx
Mean	xx.x	xx.x
SD	xx.xx	xx xx
Median	xx.x	xx.x
Min.	x	x
Max.	xx	Xx
Alanine aminotransferase (IU/L)		
n	xxx	xxx
Mean	xx.x	xx.x
SD	xx.xx	xx xx
Median	xx.x	xx.x
Min.	x	x
Max.	xx	Xx
Aspartate aminotransferase (IU/L)		
n	xxx	xxx
Mean	xx.x	xx.x
SD	xx.xx	xx xx
Median	xx.x	xx.x
Min.	x	x
Max.	xx	Xx

Programming note: include all measured blood chemistry parameters. Only albumin, ALT, and AST are shown above for illustrative purposes.

Programming note: Same format for Table 3.31 (Summary of Hematology Results at Screening). Include all collected hematology parameters.

<user ID: pathname datestamp timestamp>

Example: SAF_T07
Protocol: 207626
Population: Intent-to-Treat

Table 3.32
Summary of Vital Signs

	Treatment	N	Visit	n	Mean	SD	Median	Min.	Max.
Systolic Blood Pressure (mmHg)	FF/UMEC/VI 100/62.5/25	xxx	Screening	xxx	xxx.x	xx.xx	xxx.x	xxx	xxx
			Day 84	xxx	xxx.x	xx.xx	xxx.x	xxx	xxx
	TIO 18	xxx	Screening	xxx	xxx.x	xx.xx	xxx.x	xxx	xxx
			Day 84	xxx	xxx.x	xx.xx	xxx.x	xxx	xxx
Diastolic Blood Pressure (mmHg)	FF/UMEC/VI 100/62.5/25	xxx	Screening	xxx	xxx.x	xx.xx	xxx.x	xxx	xxx
			Day 84	xxx	xxx.x	xx.xx	xxx.x	xxx	xxx
	TIO 18	xxx	Screening	xxx	xxx.x	xx.xx	xxx.x	xxx	xxx
			Day 84	xxx	xxx.x	xx.xx	xxx.x	xxx	xxx
Heart rate (beats/min)	FF/UMEC/VI 100/62.5/25	xxx	Screening	xxx	xxx.x	xx.xx	xxx.x	xxx	xxx
			Day 84	xxx	xxx.x	xx.xx	xxx.x	xxx	xxx
	TIO 18	xxx	Screening	xxx	xxx.x	xx.xx	xxx.x	xxx	xxx
			Day 84	xxx	xxx.x	xx.xx	xxx.x	xxx	xxx

Programming note: Same format for Table 3.33 (Summary of Change from Baseline Vital Signs), but without row for Screening. Include early withdrawal and unscheduled visit data, if available, in both Tables 3.32 and 3.33.

<user ID: pathname datestamp timestamp>

Example: SAF_T08
Page 1 of 1
Protocol: 207626
Population: Intent-to-Treat

Table 3.34
Summary of ECG Findings at Screening

	FF/UMEC/VI 100/62.5/25 (N=xxx)	TIO 18 (N=xxx)
n	xxx	xxx
Normal	xx (xx%)	xx (xx%)
Abnormal – not clinically significant	xx (xx%)	xx (xx%)
Abnormal – clinically significant	xx (xx%)	xx (xx%)
Unable to evaluate	xx (xx%)	xx (xx%)

<user ID: pathname datestamp timestamp>

10.10.2. Listings

Example: POP_L01 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 11
Listing of COPD Concomitant Medications

Country: xxx
Treatment: xxxxxxxxxxxx

Centre ID/ Subject	Respiratory class/ Ingredient/ Verbatim text/ Indication	Dose/ Units/ Freq/ Route	Date started/ Study day/ Date stopped/ Study day	Taken prior to study?/ Ongoing medication?/ Treatment periods taken in	Administered for an exacerbation?/ Exacerbation severity/ Exacerbation start date
xxxxxx/ xxxxxx	xxxxxxxxxxxxx/ xxxxxxxxxxxxxxxx/ xxxxxxxxxxxxx/ xxxxxxxxxxxxxxx	xxxx/ xxxxx/ xxx/ xxxxxxx	xxxxxxxxxx/ xx/ xxxxxxxxxx/ xx	xxx/ xxx/ xxxxxxxxxx	xxx/ xxxxxxxxxx/ xxxxxxxxx

Note: Combination products are listed by individual ingredient in all applicable Respiratory Medication Classes.
<user ID: pathname datestamp timestamp>

Example: POP_L02 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 12
Listing of Non-COPD Concomitant Medications

Country: xxx
Treatment: xxxxxxxxxxxx

Centre ID/ Subject	ATC level 1/ Ingredient/ Verbatim text/ Indication	Dose/ Units/ Freq/ Route	Date started/ Study day/ Date stopped/ Study day	Taken prior to study?/ Ongoing medication?/ Treatment periods taken in
xxxxxx/ xxxxxxxxx	xxxxxxxxxxxx/ xxxxxxxxxxxxxxx/ xxxxxxxxxxxx/ xxxxxxxxxxxxxx	xxxx/ xxxxx/ xxx/ xxxxxxx	xxxxxxxxxx/ xx/ xxxxxxxxxx/ xx	xxx/ xxx/ xxxxxxxxxx, xxxxxxx, xxxxxxxxxxxx

Note: Combination products are listed by individual ingredient in all applicable Respiratory Medication Classes.
<user ID: pathname datestamp timestamp>

Example: SAF_L01
Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 13
Listing of Exposure Data

Country: xxx
Treatment: xxxxxxxxxxx

Centre ID	Subject	Exposure start date	Exposure end date	Date of Week 12 visit	Date of study completion/ withdrawal	Duration of exposure (days) [1]	Post-treatment duration (days) [2]
xxxxxx	xxxxxxxx	xxxxxxx	xxxxxxx	xxxxxxx	xxxxxxxx	xxx	xx

[1]: Calculated as ((exposure end date – exposure start date) + 1).
[2]: Calculated as (date of study completion/withdrawal – exposure end date).

<user ID: pathname datestamp timestamp>

Example: POP_L18
Page 1 of x
Protocol: 207626
Population: All Subjects Enrolled

Listing 22
Listing of Unique Subject ID vs. Study Subject ID

Country: xxxxxx

Centre ID	Treatment	Unique Subject ID	Study subject ID
xxx	xxxxxxxxx	xxxxxx.xxxxxx	Xxxxxx.xxxxxx

<user ID: pathname datestamp timestamp>

Example: POP_L03 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 23
Listing of Study Treatment Misallocations

Country: xxx

Treatment	Centre ID	Subject	Study day [1]	Date of dosing Start [2]	Date of dosing End [2]	Container number	Actual treatment dispensed
xxx.xxxxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

[1] Day, relative to randomization, on which treatment was dispensed.
[2] Dates on which actual treatment was dispensed or returned.

<user ID: pathname datestamp timestamp>

Example: POP_L04 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 24
Listing of Screening Lung Function, Reversibility Status, and GOLD Grade

Country: xxx
Treatment: xxx
Centre ID: xxx

Subject	Visit / Visit date/ Study day	Planned relative time	Actual time	FEV_1 (L)	FVC (L)	Percent predicted FEV_1 (%)	Reversibility to salbutamol (mL) /)%)	FEV_1/FVC	GOLD grade
xxx.xxxxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

<user ID: pathname datestamp timestamp>

Example: POP_L05 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 25
Listing of Medical Conditions

Country: xxx

Centre ID	Subject	Treatment	Body system	Condition	Current or Past?
xxxx	xxx.xxxx	xxxx	xxxx	xxxx	Current
			xxxx	xxxx	Past

<user ID: pathname datestamp timestamp>

Example: POP_L06
Protocol: 207626
Population: Intent-to-Treat

Listing 26
Listing of Family History of Cardiovascular Risk Factors

Country: xxx

			Family History [1]		
Treatment	Centre ID	Subject	Premature coronary artery disease [2]	Myocardial infarction	Stroke
xxx	xxx	xxx.xxxx	<yes/no>	<yes/no>	<yes/no>

[1] Family history in first degree relatives only (e.g. biological parent, sibling, or offspring).
[2] Family history of premature coronary artery disease in women < 65 years or men < 55 years in first degree relatives only.

<user ID: pathname datestamp timestamp>

Example: POP_L07
Protocol: 207626
Population: Intent-to-Treat

Listing 27
Listing of COPD Duration and Exacerbation History

Country: xxx

			Number of exacerbations in past 12 months		
			Moderate	Severe	Total moderate/severe
Treatment	Centre ID	Subject			
xxx	xxx	xxx.xxxx	x	x	x

Note: Moderate exacerbations are defined as exacerbations that required treatment with oral or systemic corticosteroids and/or antibiotics (not involving hospitalization). Severe exacerbations are defined as exacerbations that required in-patient hospitalization.

<user ID: pathname datestamp timestamp>

Example: POP_L08
Protocol: 207626
Population: Intent-to-Treat

Listing 28
Listing of Smoking History and Smoking Status

Country: xxx
Treatment: xxx

Centre ID / Subject	Visit	Years smoked / Cigarettes per day	Smoking pack-years [1]	Smoking status	Change in status?	Status change / Date change made / Study day
xxx / xxx.xxx	Screening	xx / xx	xx.x	<current / former>		xx / xx / xx
	Day 84	xx / xx	xx.x	<current / former>	<yes / no>	xx / xx / xx

Programming note: include early withdrawal and unscheduled visit data if available.

<user ID: pathname datestamp timestamp>

Example: POP_L09 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 29
Relationship between ATC Level 1, Ingredient, and Verbatim Text for Non-COPD Medications

ATC Level 1	Ingredient	Verbatim text
xxxx	xxx	xxx
		xxx
xxx	xxx	xxx

<user ID: pathname datestamp timestamp>

Example: POP_L10 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 30
Listing of Treatment Compliance Data

Country: xxx
Treatment: xxx

Centre ID	Subject	Study Phase	Overall compliance (%)	ELLIPTA compliance (%)	Handihaler compliance (%)
xxx	xxx.xxxx	Run-in Study treatment	xx.x	xx.x	xxx.

Note: Compliance values for each device are only calculated for subjects with complete treatment dispensing information.

<user ID: pathname datestamp timestamp>

Example: EFF_L01 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 31
Listing of Raw FEV_1 (L) and FVC (L) Data

Country: xxx
Treatment: xxx
Centre ID: xxx

Subject	Visit/ Visit date/ Study day	Study phase	Planned relative time	Actual time	Baseline FEV1(L)	FEV1 (L)/ Change from baseline FEV1 (L)	Baseline FVC (L)	FVC (L)/ Change from baseline FVC (L)
xxxxxxxx	xxxxx/ xxxxx/ xxx	xxxxxxxx	xxxxxxxxxxx	xxxxxx	x.xxx	x.xxx	x.xxx	x.xxx

<user ID: pathname datestamp timestamp>

Example: EFF_L02
Protocol: 207626
Population: Intent-to-Treat

Listing 32
Listing of COPD Exacerbations

Country: xxx
Treatment: xxx

Centre ID / Subject	Date of onset / Study day	Study phase at onset	Date of resolution or death / Duration (days)	Outcome	Corticosterois taken? / Antibiotics taken? / Visited ER? / Hospitalized?
xxxx / xxx.xxxx	xxx / xxx	xxx	xxx / xxx	xxx	xxx / xxx / xxx / xxx

<user ID: pathname datestamp timestamp>

Example: EFF_L03
Protocol: 207626
Population: Intent-to-Treat

Listing 33
Listing of SGRQ Scores

Country: xxx
Treatment: xxx

Centre ID / Subject	Language	Visit date / Study day	Study phase	Baseline symptoms score	Symptoms score / Change from baseline	Baseline activity score	Activity score / Change from baseline	Baseline impacts score	Impacts score / Change from baseline
xxx / xxx.xxxx	xxx	xxx / xxx	xxx	xxx	xxx / xxx	xxx	xxx / xxx	xxx	xxx / xxx

Note: Responders are defined as those subjects whose SGRQ total score is 4 units or more below baseline. Non-responders are defined as those subjects whose SGRQ total score is more than 4 units below baseline or a missing SGRQ total score at a the timepoint in question and no subsequent on-treatment scores. Subjects will not be assigned a responder status at any timepoint if their baseline SGRQ total score is missing. Subjects will not have a responder status assigned at a given timepoint if the SGRQ total score at that timepoint is missing.

Programming note: Adjust distribution of columns across pages as necessary.

<user ID: pathname datestamp timestamp>

Example: EFF_L03
Protocol: 207626
Population: Intent-to-Treat

Listing 33
Listing of SGRQ Scores

Country: xxx
Treatment: xxx

Centre ID / Subject	Language	Visit date / Study day	Baseline total score	Total score / Change from baseline	Responder? [1]
xxx / xxx.xxxx	xxx	xxx / xxx	xxx	xxx	<yes / no>

Note: Responders are defined as those subjects whose SGRQ total score is 4 units or more below baseline. Non-responders are defined as those subjects whose SGRQ total score is more than 4 units below baseline or a missing SGRQ total score at a the timepoint in question and no subsequent on-treatment scores. Subjects will not be assigned a responder status at any timepoint if their baseline SGRQ total score is missing. Subjects will not have a responder status assigned at a given timepoint if the SGRQ total score at that timepoint is missing.

Programming note: Adjust distribution of columns across pages as necessary.

<user ID: pathname datestamp timestamp>

Example: EFF_L04
Protocol: 207626
Population: Intent-to-Treat

Listing 34
Listing of CAT Scores

Country: xxx
Treatment: xxx

Centre ID / Subject	Language	Visit date / Study day	Baseline CAT score	CAT score / Change from baseline	Responder? [1]
xxx / xxx.xxxx	xxx	xxx / xxx	xxx	xxx	<yes / no>

[1] Responders are defined as those subjects whose CAT score is 2 units or more below baseline. Non-responders are defined as those subjects whose CAT score is more than 2 units below baseline or who have a missing CAT score at a the timepoint in question and no subsequent on-treatment scores. Subjects will not be assigned a responder status at any timepoint if their baseline CAT score is missing. Subjects will not have a responder status assigned at a given timepoint if the *CAT* score at that timepoint is missing.

<user ID: pathname datestamp timestamp>

Example: SAF_L02
Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 35
AE Terms of Special Interest

Special Interest Term	Subgroup	Preferred Term
xxxxxxxxx	xxxxxxxx	xxxxxxx
		xxxxxxxxxxx
xxxxxxxxxxxxx	xxxxxxxxx	xxxxxxxxxxxxxxx

Note: All of the pre-specified preferred terms that were assigned to special interest terms are shown, regardless of whether they actually occurred in the study.

<user ID: pathname datestamp timestamp>

Example: SAF_L03 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 37
Listing of Pneumonia Data

Country: xxx
Treatment: xxx

Centre ID / Subject	Date of onset / Study phase at onset / Supported by X-ray or CT scan?	eCRF question	Response
xxx / xxx.xxxx	xxx / xxx / xxx / xxx	Level of cough	<yes / no / unknown>
		Increased sputum purulence?	
		Did the chest auscultation show evidence of crackles / rales and / or bronchial or brochovesicular breath sounds?	
		Worsening dyspnea?	
		Does subject have pleural effusion?	
		Does subject have hypoxemia?	
		Was WBC count assessed at time of event?	
		Was BUN > 19mg/dL (7mmol / L)?	
		Was there evidence of subject confusion?	
		Was subject in an inpatient health care setting when pneumonia developed?	
		Was a culture or swab taken?	

<user ID: pathname datestamp timestamp>

Example: SAF_L04 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 38
Listing of Bone Fracture Data

Country: xxx
Treatment: xxx

Centre ID / Subject	Fracture date / Study phase	Fracture type	Side	Fracture location
xxx / xxx.xxxx	xxx / xxx	xxx	<left / right>	

<user ID: pathname datestamp timestamp>

Example: SAF_L05
Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 39
Listing of Chest Imaging (X-ray or CT scan) Data

Country: xxx
Treatment: xxx

Centre ID/ Subject	Date of image/ Study phase/ Study day	Associated with pneumonia	Associated with moderate/severe exacerbation	Consistent with diagnosis of pneumonia
xxxxxx/ xxxxxx	xxxxxxx/ xxxxxxxxxx/ xxx	xxx	xxx	xxx

Note: A chest x-ray/CT scan is associated with pneumonia if it is taken during the pneumonia or within -7 to +10 days (inclusive) of the date of onset.
Note: A chest x-ray/CT scan is associated with a moderate/severe exacerbation if it is taken during the exacerbation or within -7 to +10 days (inclusive) of the date of onset.

<user ID: pathname datestamp timestamp>

Example: SAF_L06 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 40
Listing of Liver Event Results and Time of Event Relative to Treatment

Country: xxx
Treatment: xxx

Centre ID / Subject	Age (y) / Sex / Race	Maximum status of the liver event	Date first detected / Study phase at event onset / Study day	Days from first dose to start of event	Days from last dose to start of event	Restart / rechallenge after stopping criteria were met?	Outcome / Date resolved
xxx / xxx	xxx / xxx / xxx	xxx	xxx / xxx / xxx	xxx	xxx	xxx	xxx / xxx

<user ID: pathname datestamp timestamp>

Example: SAF_L07 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 41
Listing of Medical Conditions for Subjects with Liver Stopping Events

Country: xxx
Treatment: xxx

Centre ID / Subject	Age (y) / Sex / Race	Condition	Status
xxx / xxx	xxx / xxx / xxx	Acute Viral Hepatitis A	<current/past/no medical condition/not assessed>
		Acute hepatitis B	
		Chronic hepatitis B	
		Hepatitis B carrier	
		Chronic hepatitis C	
		Cytomegalovirus hepatitis	
		Epstein-Barr virus infectious mononucleosis	
		Herpes simplex hepatitis	
		Alcoholic liver disease	
		Non-alcoholic steatohepatitis	
		Fatty liver	
		Hepatic cirrhosis	
		Hemochromatosis	
		Autoimmune hepatitis	
		Gallbladder disease	
		Hepatobiliary cancer	
		Liver metastasis	
		Hepatitis E IgM antibody	
		Drug-related liver disease	
		Other condition (specify)	

Drug allergies

<user ID: pathname datestamp timestamp>

Example: SAF_L07
Protocol: 207626
Population: Intent-to-Treat

Listing 41
Listing of Medical Conditions for Subjects with Liver Stopping Events

Country: xxx
Treatment: xxx

Centre ID / Subject	Age (y) / Sex / Race	Condition	Status
xxx / xxx	xxx / xxx / xxx	Rheumatoid arthritis	<current/past/no medical condition/not assessed>
		Psoriasis	
		Thyroid disease	
		Inflammatory bowel disease	
		Lupus	
		Sjogren's syndrome	
		Vilitigi	

<user ID: pathname datestamp timestamp>

Example: SAF_L08 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 42
Listing of Substance Use for Subjects with Liver Stopping Events

Country: xxx
Treatment: xxx

Centre ID / Subject	Age (y) / Sex / Race	Date of assessment	Does subject consume alcohol?	If yes, avg number of units consumed per week
xxx / xxx	xxx / xxx / xxx	ddMMMyyyy	<yes/no>	xxx

<user ID: pathname datestamp timestamp>

Example: SAF_L09
Protocol: 207626
Population: Intent-to-Treat

Listing 43
Listing of Liver Event Information for RUCAM Scores

Country: xxx
Treatment: xxx

Centre ID / Subject	Age (y) / Sex / Race	Liver stopping event date	Serious AE? / If female, pregnant?	Diagnostic tests performed? / If so, normal?	Liver biopsies performed?	Use of herbals, supplements, ilicit drugs? / Dietary change in past week?	Criterion/ criteria met
xxx / xxx	xxx / xxx / xxx	ddMMMyyyy	<yes / no> / <yes / no>	<yes / no> / <yes / no>	<yes / no>	<yes / no> / <yes / no>	*list all criteria checked*

<user ID: pathname datestamp timestamp>

Example: SAF_L10

Protocol: 207626
Population: Intent-to-Treat

Listing 44
Listing of Liver Biopsy Details

Country: xxx
Treatment: xxx

Centre ID / Subject	Age (y) / Sex / Race	Date of biopsy	Appx size of biopsy (unit)	Final diagnosis	Final diagnosis details	Liver architecture	Liver architecture details
xxx / xxx	xxx / xxx / xxx				*If "Final diagnosis" is "Abnormal," list all conditions that apply.*		*If "Liver architecture" is "Abnormal," list all conditions that apply*

<user ID: pathname datestamp timestamp>

Listing 44
Listing of Liver Biopsy Details

Country: xxx
Treatment: xxx

Centre ID / Subject	Age (y) / Sex / Race	Date of biopsy	Description of liver cells or hepatocytes	Description of liver cells or hepatocytes details	Liver cell or hepatocyte inclusions or vacuoles	Liver cell or hepatocyte inclusions or vacuoles details
xxx / xxx	xxx / xxx / xxx			*If "Description of liver cells or hepatocytes" is "abnormal," list all conditions that apply.*		*If "Liver cell or hepatocyte inclusions or vacuoles," is answered, list all conditions that apply*

<user ID: pathname datestamp timestamp>

Listing 44
Listing of Liver Biopsy Details

Country: xxx
Treatment: xxx

Centre ID / Subject	Age (y) / Sex / Race	Date of biopsy	Hepatocyte or liver cell nuclear abnormalities	Hepatocyte or liver cell nuclear abnormalities details	Liver or lobular infiltrates	Liver or lobular infiltrates details
xxx / xxx	xxx / xxx / xxx			*If "Hepatocyte or liver cell abnormalities" is "Yes," list all conditions that apply.*		*If "Liver or lobular infiltrates" is "Yes," list all conditions that apply*

<user ID: pathname datestamp timestamp>

Example: SAF_L10
Protocol: 207626
Population: Intent-to-Treat

Listing 44
Listing of Liver Biopsy Details

Country: xxx
Treatment: xxx

Centre ID / Subject	Age (y) / Sex / Race	Date of biopsy	Portal tract inflammation	Portal tract inflammation details	Bile ducts	Bile ducts details
xxx / xxx	xxx / xxx / xxx			*If "Portal tract inflammation" is "Yes," list all conditions that apply.*		*If "Bile ducts" is "Abnormal," list all conditions that apply*

<user ID: pathname datestamp timestamp>

Listing 44
Listing of Liver Biopsy Details

Country: xxx
Treatment: xxx

Centre ID / Subject	Age (y) / Sex / Race	Date of biopsy	Portal veins	Portal veins details	Liver infections	Liver infections details
xxx / xxx	xxx / xxx / xxx			*If "Portal veins" is "Abnormal," list all conditions that apply.*		*If "Liver infections" is "Abnormal," list all conditions that apply*

<user ID: pathname datestamp timestamp>

Listing 44
Listing of Liver Biopsy Details

Country: xxx
Treatment: xxx

Centre ID / Subject	Age (y) / Sex / Race	Date of biopsy	Parasites or ova	Parasites or ova	Histologic staining or additional studies?	Histologic staining or additional studies details
xxx / xxx	xxx / xxx / xxx			*If "Parasites or ova" is "Yes," list all conditions that apply.*		*If "Histologic staining or additional studies?" is "Yes," list all items that apply.*

<user ID: pathname datestamp timestamp>

Example: SAF_L11 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 45
Listing of Liver Imaging Details

Centre ID / Subject	Age (y) / Sex / Race	Date of hepatic or liver imaging	Method used / Adequate images?	Liver size / texture / infiltration grade	Accites present?	Hepatic lesions?	Biliary ductal leisions?	Portal or hepatic vein abnormalities?
xxx / xxx	xxx / xxx / xxx	ddMMMyyyy	xxx / xxx	xxx / xxx / xxx	xxx	*List all that apply*	*List all that apply*	*List all that apply*

<user ID: pathname datestamp timestamp>

Example: SAF_L12
Protocol: 207626
Population: Intent-to-Treat

Listing 46
Listing of Inhaler Malfunctions

Country: xxx
Treatment: xxx

Centre ID	Subject	Age (y) / Sex / Race	Container number	Malfunctioning device type	Malfunction comment / Reason for device malfunction
xxx	xxx.xxxx	xxx / xxx / xxx	Xxx	xxx	xxx / xxx

<user ID: pathname datestamp timestamp>

Example: SAF_L14
Protocol: 207626
Population: Intent-to-Treat

Listing 47
Listing of Hepatitis B and C Test Results

Country: xxxxxx
Treatment: xxxxxxxx

Centre ID	Subject	Study phase/ Visit/ Visit date	Hepatitis B surface antigen	Hepatitis C antibody
xxxxxx	xxxxxx	xxxxxxxxxxx/ xxxxxxxxxx/ xxxxxx	xxxxxxxxxxxx	xxxxxxxxxxxxx

Example: SAF_L15
Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Listing 48
Listing of ECG Data

Country: xxxxxx
Treatment: xxxxxxxx

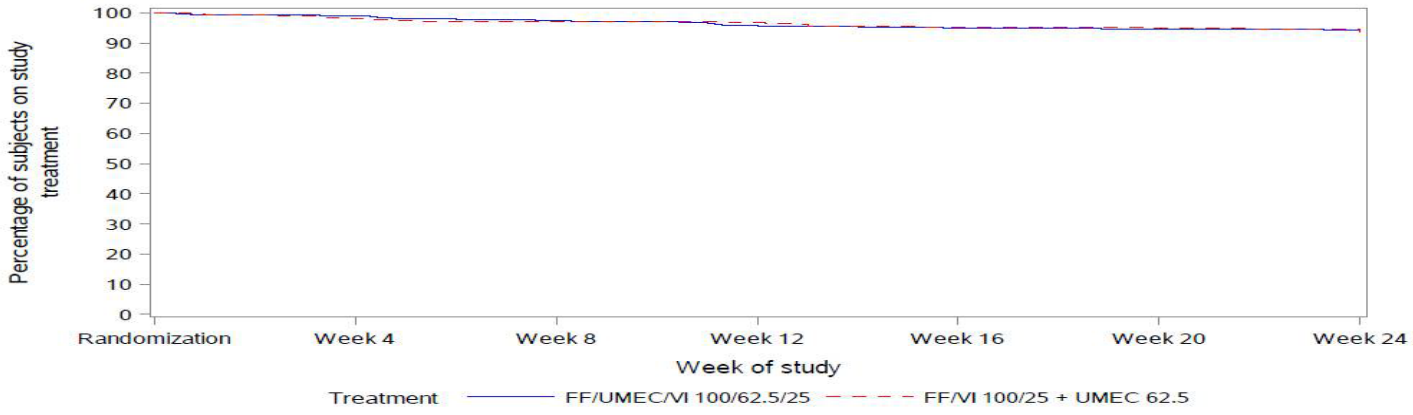
Centre ID	Subject	Visit/ Visit date/ Study phase/ Study day	Result	Abnormality
xxxxxx	xxxxxx	xxxxxxx/ xxxxxxxx/ xxxxxxxxxx/ xx	<Normal / Abnormal – not clinically significant / Abnormal – clinically significant>	xxxxxxxxxxxxx xx

<user ID: pathname datestamp timestamp>

10.10.3. Figures

Example: POP_F01 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Figure 1.2
Kaplan-Meier Plot of Time to Study Withdrawal



Number of subjects remaining in study							
FF/UMEC/VI 100/62.5/25	527	521	513	505	501	496	339
FF/VI 100/25 + UMEC 62.5	528	518	513	511	502	500	338

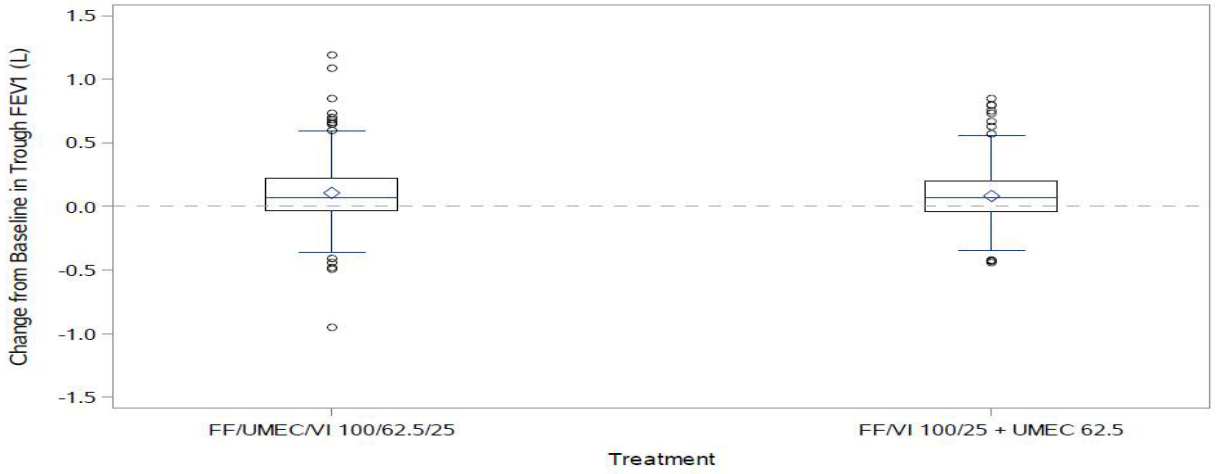
Note: Subjects who complete the treatment period are censored at the date of study treatment completion or day 168 whichever is the earliest.

PPD

Programming note: same format for Figure 1.2 (Kaplan-Meier Plot of Time to Study Treatment Discontinuation)

Example: EFF_F01 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Figure 2.1
Box Plot of Change from Baseline in Trough FEV_1 (L) on Day 85 – Hypothetical Estimand



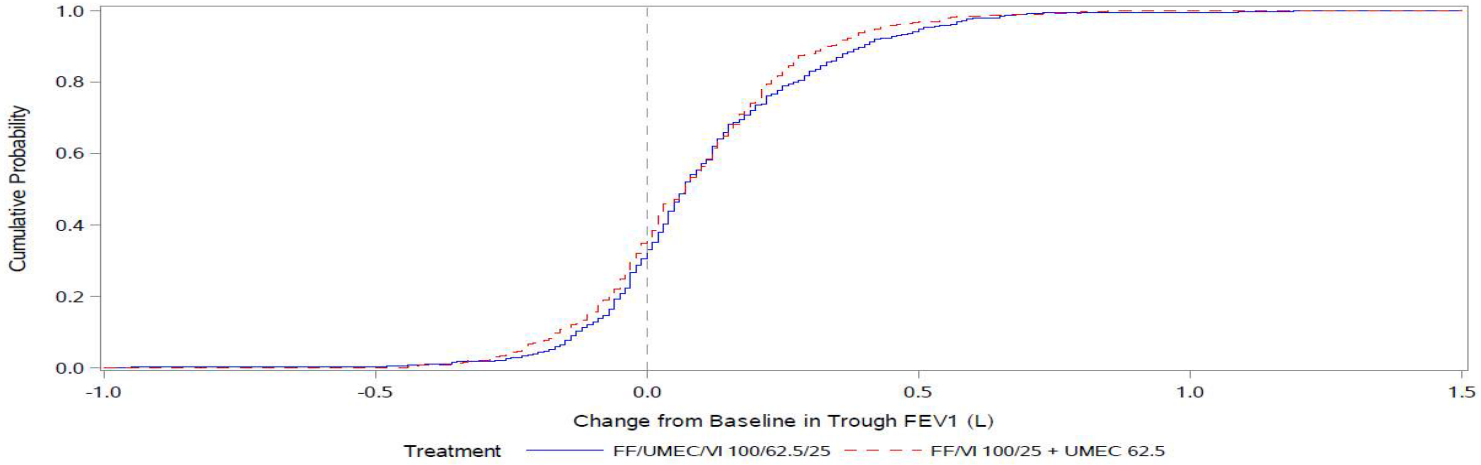
PPD

Programming note: same format for Figure 2.4 (Box Plot of Change from Baseline in Trough FEV_1 (L) on Day 85 – Treatment Policy Estimand)

Example: EFF_F02 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Figure 2.2

Empirical Distribution Function Plot of Change from Baseline in Trough FEV1 (L) on Day 85 – Hypothetical Estimand

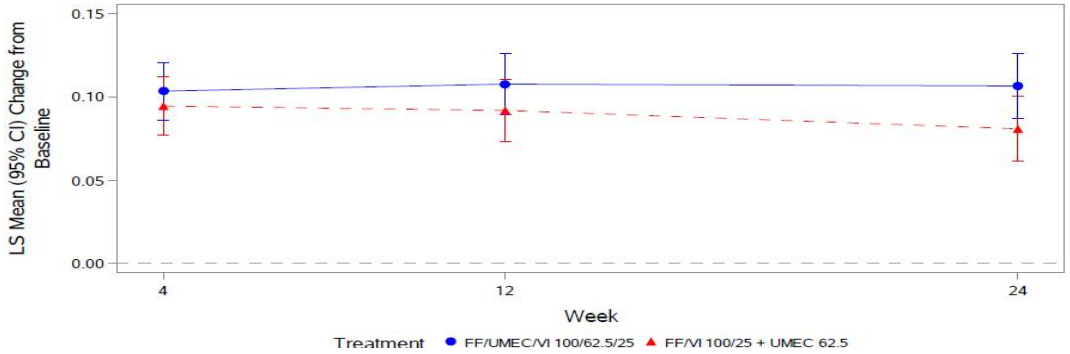


PPD

Programming note: same format for Figure 2.5 (Empirical Distribution Function Plot of Change from Baseline in Trough FEV1 (L) on Day 85 -- treatment policy estimand), Figure 2.7 (Empirical Distribution Function Plot of Change from Baseline in SGRQ Total Score on Day 84 – Hypothetical Estimand), and Figure 2.9 (Empirical Distribution Function Plot of Change from Baseline in CAT Score on Day 84 – Hypothetical Estimand

Example: EFF_F03 Page 1 of x
Protocol: 207626
Population: Intent-to-Treat

Figure 2.3
Least Squares Mean (95% CI) Change from Baseline in Trough FEV1 (L) – Hypothetical Estimand



Note:Analysis performed using a repeated measures model with covariates of baseline FEV1, stratum (number of long-acting bronchodilators per day during the run-in: 0/1 or 2), visit, geographical region, treatment, visit by treatment and visit by baseline interaction.

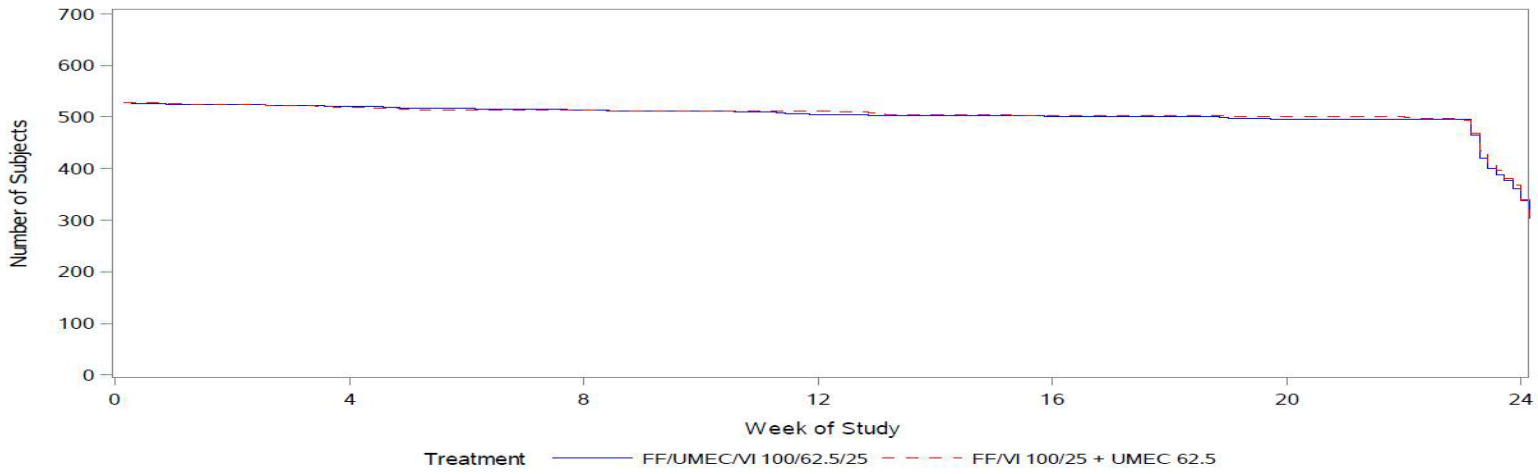
PPD

Programming note: same format for Figure 2.6 (Least Squares Mean (95% CI) Change from Baseline in Trough FEV1 (L) – Treatment Policy Estimand), Figure 2.8 (Least Squares Mean (95% CI) Change from Baseline in SGRQ Total Score – Hypothetical Estimand), and Figure 2.10 (Least Squares Mean (95% CI) Change from Baseline in CAT Score – Hypothetical Estimand

Programming note: Footnotes for Figures will be study-specific; those shown above are illustrative only.

Example: SAF_F01
Protocol: 207626
Population: Intent-to-Treat

Figure 3.1
Summary of Treatment Exposure



PPD

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