Reporting and Analysis Plan

Study ID: 107116

Official Title of Study: Reporting and Analysis Plan for HZA107116: A doubleblind, parallel group study to evaluate the safety and efficacy of fluticasone furoate/vilanterol combination compared to fluticasone furoate in the treatment of asthma in participants (aged 5 to 17 years old inclusive)

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Title	:	Reporting and Analysis Plan for HZA107116: A double-blind, parallel group study to evaluate the safety and efficacy of fluticasone furoate/vilanterol combination compared to fluticasone furoate in the treatment of asthma in participants (aged 5 to 17 years old inclusive)
Compound Number	:	GW685698+GW642444
Effective Date	:	Refer to Document Date

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report (CSR) for Protocol HZA107116.
- This RAP is intended to describe the study population, efficacy and safety analyses required for the study.
- This version of the RAP includes amendments to the originally approved RAP
- This RAP will be provided to the study team members to convey the content of the final Statistical Analysis Complete (SAC) deliverable.

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1. INTRODUCTION

The purpose of this RAP is to describe the analyses and output to be included in the CSR for Protocol HZA107116:

Revision Chronology:		
2016N298634_00	22-JUN-2017	Original
2016N298634_01	19-JUN-2019	Amendment 1
2016N298634_02	10-DEC-2019	Amendment 2
2016N298634_03	31-JAN-2020	Amendment 3
2016N298634_04	24-AUG-2020	Amendment 4

1.1. RAP Amendments

This amendment has been made in order to add the following additional data displays:

- 2 additional efficacy tables that were requested by the FDA (Table 2.77 and Table 2.78)
- 3 additional study population tables (Table 1.67, Table 1.68 and Table 1.69), 1 additional safety table (Table 3.72) and 2 additional listings (Listing 31 and 32) that summarise the impact of the COVID-19 pandemic on the study

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

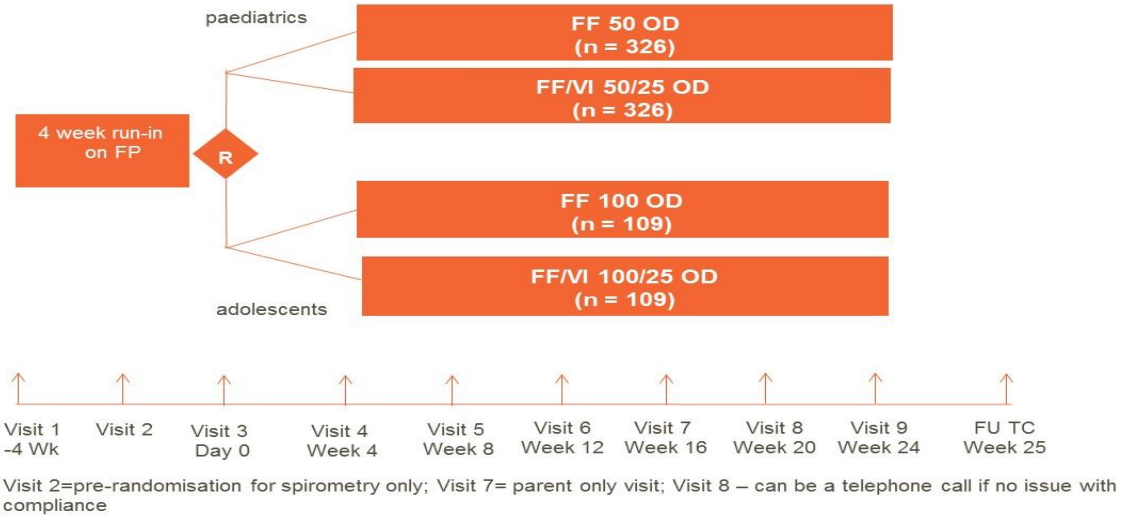
There are no changes or deviations to the originally planned statistical analysis specified in the protocol [GlaxoSmithKline Document Number: 2016N298634_00 (Dated: 22JUN2017)].

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

<table>
<tr><th>Objective</th><th colspan="2">Endpoint</th></tr>
<tr><td colspan="3">Primary</td></tr>
<tr><td rowspan="2"><u>Common to both 5-11 and 5-17 years population</u>
• To compare the efficacy of once daily FF/VI with once daily FF in participants with asthma.
The primary estimand is that of treatment policy (effectiveness-type estimand). The secondary efficacy-type estimand will be defined for the primary and powered secondary endpoints.</td><td><u>Primary endpoint for 5-11 years population</u>
• Change from baseline, averaged over weeks 1-12 of the treatment period, in pre-dose (i.e. trough) morning peak expiratory flow (PEF), captured daily via electronic patient diary. This is a secondary endpoint for the 5-17 years population.</td><td><u>Primary endpoint for 5-17 years population</u>
• Weighted mean FEV_1 (0-4 hours) at week 12. This is a secondary endpoint for the 5-11 years population.</td></tr>
<tr><td colspan="2"><u>Secondary endpoints common to both 5-11 and 5-17 years population:</u>
• Change from baseline in the percentage of rescue-free 24-hour periods over weeks 1-12 of the treatment period (powered secondary endpoint for 5-11 years population) captured daily via electronic patient diary.
• Change from baseline in the percentage of symptom-free 24-hour periods over weeks 1-12 of the treatment period, captured daily via electronic patient diary.
• Change from baseline in morning (AM) forced expiratory flow in 1 second (FEV_1) in participants who can perform the manoeuvre at week 12.
• Change from baseline in Asthma Control Questionnaire (ACQ-5) at week 24.
• Incidence of exacerbations over the 24 week treatment period.
<u>Other endpoints common to both 5-11 and 5-17 years population:</u>
• Change from baseline, averaged over weeks 1-12 of the treatment period in evening (PM) PEF, captured daily via</td></tr>
</table>

Objective	Endpoint
	electronic patient diary.
Secondary	
<u>Common to both 5-11 and 5-17 years population</u> • To assess the safety of FF/VI in participants with asthma	• Incidence of adverse events (AEs). • Evaluation of electrocardiogram (ECG) at screening and end of treatment. • Evaluation of fasting blood glucose pre- and post-treatment.

2.3. Study Design

Overview of Study Design and Key Features	
 Visit 2=pre-randomisation for spirometry only; Visit 7= parent only visit; Visit 8 – can be a telephone call if no issue with compliance	
Design Features	• HZA107116 is a randomized, double-blind, stratified, parallel group, multicenter study evaluating the efficacy and safety of once daily fluticasone furoate/vilanterol (FF/VI) inhalation powder compared to once daily fluticasone furoate (FF) inhalation powder in the treatment of asthma in participants aged 5 to 17 years old currently uncontrolled on inhaled corticosteroids (ICS). • Participants meeting the screening criteria at Visit 1 will receive fluticasone propionate (FP) 100 mcg twice daily during the 4-week open-label run-in period. Participants meeting the randomization eligibility criteria at Visit 3 will be randomized to receive one of two blinded study treatments. • Participants will be supplied with albuterol/salbutamol (inhalation aerosol or nebulizer) to use as needed throughout the study. • Participants will receive study treatment for 24 weeks (168 days). A follow-up telephone contact will be performed one week after completing study medication. Participants will therefore participate in the study for up to a maximum of 29 weeks. • Participants are required to attend the clinic between 6am and 11am at each visit, except for Visits 7 and 8 and the follow-up visit. Visit 7 can be a parent only visit, Visit 8 can be a telephone call if there are no issues with compliance, and the follow-up visit (Visit 10) will be conducted via a telephone call. • Only participants completing the treatment and follow-up periods will be considered to have completed the study. • Participants who discontinue blinded study treatment will not be automatically withdrawn, but will be encouraged to stay in the study and complete all remaining protocol specified visits and be followed-up as per the protocol until the completion of the follow-up assessments. • Further details of the study design can be found in Section 5 of the HZA107116 protocol [GlaxoSmithKline Document Number 2016N298634_00].
Time & Events	• Refer to Appendix 2: Schedule of Activities.
Treatment Assignment	• Randomization to once daily (OD) blinded study treatment will be stratified by the participant's age at the screening visit (5 to 11 years and 12 to 17 years). • Participants 5 to 11 will be randomized in a 1:1 ratio to one of the two following

Overview of Study Design and Key Features	
	treatments: ○ FF 50 OD ○ FF/VI 50/25 OD • Participants 12 to 17 will be randomized in a 1:1 ratio to one of the two following treatments: ○ FF 100 OD ○ FF/VI 100/25 OD • Study treatment will be delivered by the ELLIPTA Dry Powder Inhaler (DPI). The ELLIPTA DPI will contain 30 doses (FF/VI or FF). Participants will be instructed to administer the ELLIPTA DPI once daily in the morning for the duration of the 24-week treatment period. • The randomization schedule was generated using PAREXEL software and was stratified by age (5-11 and 12-17 years old) and used appropriate blocking of study drug. Participants will be assigned to study treatment in accordance with the randomization schedule using the PAREXEL Interactive Voice Response System (IVRS). Centralized randomization will be used for treatment allocation.
Interim Analysis	• No interim analysis is planned for this study.

2.4. Statistical Hypotheses

The primary purpose of this study is to demonstrate improvements in lung function and rescue use for participants treated with FF/VI compared with FF. For each Intent-to-Treat (ITT) population, the study is designed to show a statistically significant difference between FF/VI [ICS/long-acting beta agonist (LABA) combination therapy] and FF alone (ICS monotherapy) in the primary efficacy endpoint, thereby demonstrating the contribution of the LABA (VI).

The primary efficacy endpoint for the ITT (5-17 Years Old) Population is weighted mean FEV_1 (0-4 hours). For the ITT (5-11 Years Old) Population the primary efficacy endpoint is the change from baseline in AM PEF and the nominated powered secondary endpoint is the change from baseline in rescue-free 24-hour periods. For each of these endpoints there will be a single inequality comparison of FF/VI versus FF. Demonstration of efficacy for each of these inequality comparisons will be based on a hypothesis testing approach, whereby the null hypothesis is that there is no difference between treatment groups for the endpoint of interest and the alternative hypothesis is that there is a difference between treatment groups.

A 2-sided 5% risk associated with incorrectly rejecting any of the null hypotheses (significance level) is considered acceptable for this study. As the comparisons on the 5-17 Years Old Population and the 5-11 Years Old Population are being made for different purposes they will each have distinct multiple testing strategies which will be assessed separately. (See Section 5.5 Multiple Comparisons and Multiplicity).

3. PLANNED ANALYSES

3.1. Interim Analyses

No interim analysis is planned for this study.

3.2. Final Analyses

The final planned analyses will be performed 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 (DBR) has been declared by Data Management.
3. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed according to PAREXEL and PAREXEL Informatics procedures.
5. Database freeze (DBF) has been declared by Data Management.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Total	• All participants screened for eligibility and for whom a record exists on the study database. Included are: screen failures, run-in failures and randomized participants. • Any participant who receives a treatment randomization number will be considered to have been randomized.	• Disposition
ITT (5-17 Years Old) Population	• All randomized participants who received at least one dose of study treatment. • Randomized participants will be assumed to have received study treatment unless definitive evidence to the contrary exists. • Outcomes will be reported according to the randomized treatment allocation.	• Study population, efficacy and safety • This will constitute one of the two primary populations for all efficacy and safety analyses.
ITT (5-11 Years Old) Population	• Subset of the ITT (5-17 Years Old) Population for participants 11 years old and younger at Screening (Visit 1). • Outcomes will be reported according to the randomized treatment allocation.	• Study population, efficacy and safety • This will constitute one of the two primary populations for all efficacy and safety analyses.

Refer to Appendix 9: List of Data Displays which details the population used for each display.

4.1. Protocol Deviations

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

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan (PDMP). (See Appendix 1: Protocol Deviation Management).

- Data will be reviewed prior to unblinding and freezing of the database to ensure all important deviations are captured and categorized in the protocol deviations dataset. (Incorrect treatment deviations due to misallocation of study drug will be identified post unblinding).
- This dataset will be the basis for the summaries and listings of protocol deviations.

A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the electronic case report form (eCRF).

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
PAREXEL Informatics IVRS		Data Displays for Reporting	
Code	Description	Description	Order in Display
A	Fluticasone Furoate 50mcg once daily	FF	2
B	Fluticasone Furoate/Vilanterol 50/25mcg once daily	FF/VI	1
C	Fluticasone Furoate 100mcg once daily	FF	2
D	Fluticasone Furoate/Vilanterol 100/25mcg once daily	FF/VI	1

ICS doses (50mcg and 100mcg) within the FF/VI treatment groups and the FF treatment groups will be combined for analysis and reporting for the ITT (5-17 Years Old) Population. Treatment groups for both ITT populations will be displayed as FF/VI and FF and treatment comparisons will be displayed as FF/VI vs FF.

5.2. Baseline Definitions

Parameter	Study Assessments Considered as Baseline				Baseline Used in Data Display
	Visit 1, Screening	Day -7 to Day 1 (Pre-Dose)	Visit 2, Day -5 (Pre-Dose)	Visit 3, Day 1 (Pre-Dose)	
Efficacy					
Weighted Mean FEV_1 (0-4 hours), AM FEV_1			X		Day -5 pre-dose
AM PEF		X			Average of measurements from Day -6 to Day 1 pre-dose
PM PEF		X			Average of measurements from Day -7 to Day -1
Percentage of Rescue-Free 24-		X			Calculated from evening (Day -7 to

Parameter	Study Assessments Considered as Baseline				Baseline Used in Data Display
	Visit 1, Screening	Day -7 to Day 1 (Pre-Dose)	Visit 2, Day -5 (Pre-Dose)	Visit 3, Day 1 (Pre-Dose)	
Hour Periods, Percentage of Symptom-Free 24-Hour Periods					Day -1) and morning (Day -6 to Day 1) measurements
ACQ-5				X	Day 1
Safety					
12-Lead ECG	X				Screening
Fasting Glucose	X				Screening

Notes:

- Day 1 is referenced as Day 0 (Visit 3 / Randomization) in Section 2.3: Study Design and Appendix 2: Schedule of Activities but will be reported as Day 1 per Clinical Data Interchange Standards Consortium (CDISC) reporting guidelines.
- Unless otherwise stated, if the baseline for an endpoint is missing it will not be imputed using a different timepoint or derivation, but will remain missing.

5.3. Multicentre Studies

In this global multicentre study, enrolment will be presented by centre, country and region.

It is anticipated that many centres will enrol small numbers of participants. Consequently, all centres within the same country will be pooled. In addition, if there are any countries enrolling very small numbers in total (<12 participants in either of the ITT populations), these countries will be pooled with another country within a similar geographical region. All amalgamations will be finalized and documented prior to unblinding the treatment codes. These amalgamations will be used wherever region is incorporated into a statistical analysis.

5.4. Examination of Covariates, Other Strata and Subgroups

5.4.1. Covariates and Other Strata

Unless otherwise stated, all statistical models used for efficacy and safety analyses will be adjusted for baseline (of the analysis variable), region, sex, age and treatment group. Randomization to blinded study treatment is stratified by the participant's age at the screening visit (5 to 11 years and 12 to 17 years). Statistical models will use age at screening as a covariate and not the randomization stratum.

5.4.2. Examination of Subgroups

The following outcomes will be summarized by treatment group within subgroups defined by age, gender, race, ethnicity and geographical region:

- Demographic characteristics
- Disease characteristics
- Screening and baseline lung function test results
- Weighted mean FEV_1 (0-4 hrs) at Week 12
- Change from baseline in AM PEF over Weeks 1-12
- Change from baseline in percentage of rescue-free 24-hr periods over Weeks 1-12
- On-treatment adverse events

For the purpose of these summaries, subgroups will be defined as:

Category	Subgroups
Age Group	• ≤ 7 years old • 8-11 years old • ≥ 12 years old
Gender	• Male • Female
Race	• African American/African Heritage • American Indian or Alaska Native • Asian • Native Hawaiian or other Pacific Islander • White • Mixed Race
Ethnicity	• Hispanic or Latino • Not Hispanic or Latino
Geographical Region	• US • Non-US

Notes:

- All race subgroups will be included in the displays, but if the number of participants is small within a particular subgroup (<20 participants), it will not be discussed in the CSR.
- Details of the planned summaries are presented in Appendix 9: List of Data Displays.

5.5. Multiple Comparisons and Multiplicity

A 2-sided 5% risk associated with incorrectly rejecting any of the null hypotheses (significance level) is considered acceptable for this study. As the comparisons on the ITT (5-17 Years Old) Population and the ITT (5-11 Years Old) Population are being made for different purposes they will each have distinct multiple testing strategies which will be assessed separately.

For each of the two populations, in order to account for multiplicity across the key endpoints, a step-down closed testing procedure will be applied to the inequality comparison of FF/VI versus FF whereby this comparison will be required to be significant at the 0.05 level for the primary endpoint in order to infer on the secondary

endpoints, and inference for a test in the pre-defined hierarchy of secondary endpoints is dependent upon statistical significance having been achieved for the previous comparison in the hierarchy of secondary endpoints. If a given statistical test fails to reject the null hypothesis of no treatment difference at the significance level of 0.05, then all tests lower down in the hierarchy will be interpreted as descriptive only.

Figure 1 Statistical Testing Strategy for ITT (5-17 Years Old) Population

Testing of each endpoint is dependent on significance at the 0.05 level having been achieved on the previous endpoint in the hierarchy.	
Primary Efficacy Endpoint	
1) Weighted mean FEV_1 (0-4 hours):	FF/VI vs. FF
Secondary Efficacy Endpoints	
2) Rescue-free 24 hour periods:	FF/VI vs. FF
3) Symptom-free 24 hour periods:	FF/VI vs. FF
4) AM FEV_1:	FF/VI vs. FF
5) AM PEF:	FF/VI vs. FF
6) ACQ:	FF/VI vs. FF

Figure 2 Statistical Testing Strategy for ITT (5-11 Years Old) Population

Testing of each endpoint is dependent on significance at the 0.05 level having been achieved on the previous endpoint in the hierarchy.	
Primary Efficacy Endpoint	
1) AM PEF:	FF/VI vs. FF
Secondary Efficacy Endpoints	
2) Rescue-free 24 hour periods:	FF/VI vs. FF
3) Symptom-free 24 hour periods:	FF/VI vs. FF
4) AM FEV_1:	FF/VI vs. FF
5) ACQ:	FF/VI vs. FF
6) Weighted mean FEV_1 (0-4 hours):	FF/VI vs. FF

The treatment comparisons defined as part of the multiple testing strategy will be limited to the specified key comparisons shown in Figure 1 and Figure 2. Analyses of other efficacy measures in either population for the FF/VI versus FF treatment comparison are

nested under the secondary efficacy measures and no multiplicity adjustment is planned for these other efficacy endpoints.

In each population, if significance is achieved for the FF/VI versus FF treatment comparison on the primary efficacy endpoint, then the secondary endpoints will be tested in a closed-testing manner using the hierarchy of comparisons. If significance is also achieved for each of the secondary efficacy endpoints, then all other efficacy endpoints will be tested for the FF/VI versus FF treatment comparison without further multiplicity adjustment.

5.6. Other Considerations for Data Analyses and Data Handling Conventions

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

Section	Component
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

Study population summaries will be based on the ITT (5-17 Years Old) Population and the ITT (5-11 Years Old) Population, unless otherwise specified.

Study population summaries including summaries of participant disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, and exposure and treatment compliance will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 9: List of Data Displays.

6.2. Supplementary Information of Study Population Displays

6.2.1. Disease and Baseline Characteristics

Asthma exacerbation history (12-month history) at Screening will be summarized with frequency distributions of the number of exacerbations treated with oral/systemic corticosteroids not involving hospitalization; the number of exacerbations requiring hospitalization; and the total number of exacerbations (i.e., those not involving hospitalization and those involving hospitalization). Asthma duration and smoking history will also be summarized.

The Childhood Asthma Control Test (cACT) or Asthma Control Test (ACT) will be completed at Screening (Visit 1) and Randomization (Visit 3) as part of eligibility and randomization criteria determination. The cACT will be completed by participants 5 to 11 years old and the ACT will be completed by participants 12 to 17 years old. The cACT and ACT total scores calculated by the eCRF will be summarized.

The screening and baseline lung function summary will include Screening (Visit 1) pre- and post-bronchodilator FEV_1 and FEV_1 as a percentage of predicted normal, FVC, FEV_1/FVC as a percentage, and FEV_1 reversibility to albuterol/salbutamol (expressed as milliliters and as a percentage). Baseline FEV_1 (in liters and as a percentage of predicted normal) measured at Pre-Randomization (Visit 2) will also be summarized. These lung function measurements will be provided by an electronic data vendor and no recalculation will be performed.

6.2.2. Treatment Compliance

Calculation of treatment compliance will be based on the ELLIPTA DPI dose counter (which displays the number of doses remaining) as described in Appendix 6: Derived and Transformed Data. Treatment compliance (calculated as a percentage) will be summarized categorically and with descriptive statistics.

6.2.3. Concomitant Medications

Concomitant medications will be coded using the GSK Drug coding dictionary. Summaries of the number and percentage of participants taking concomitant medications will be displayed by ingredient without regard to Anatomical Therapeutical Chemical

(ATC) classifications. These summaries will include single-ingredient medications and will present multi-ingredient medications according to the combination of the component ingredients. Summaries will be split into asthma and non-asthma concomitant medications, as well as into those taken pre-, during, and post-treatment (as described in Section 10.4.1 Study Phases).

7. EFFICACY ANALYSES

7.1. Primary Efficacy Analyses

7.1.1. Endpoint and Summary Measure

ITT (5-17 Years Old) Population

The primary endpoint is weighted mean FEV_1 (0-4 hours) (L) at Week 12. The summary measure is the adjusted mean treatment difference at Week 12.

ITT (5-11 Years Old) Population

The primary endpoint is change from baseline in AM PEF (L/min) over Weeks 1-12. The summary measure is the adjusted mean treatment difference over Weeks 1-12.

7.1.2. Strategy for Intercurrent (Post-Randomization) Events

The primary treatment effect to be estimated is the treatment policy effect of initial randomized treatment. Intercurrent events considered to have an impact on estimation of the treatment effect are:

- Discontinuation of randomized treatment
- Increased use of rescue medication
- Withdrawal from the study

All recorded data up to the time of study withdrawal will be included in the primary analysis, regardless of discontinuation of randomized treatment or increased use of rescue medication. To minimize study withdrawals, participants who discontinue randomized treatment will be encouraged to stay in the study and complete all remaining protocol-specified visits and be followed-up as per the protocol until the completion of the follow-up assessments.

The primary efficacy analyses will include data from all participants independent of whether they had discontinued randomized treatment at the time of measurement of the primary efficacy endpoint. All non-missing data will be included in the primary analyses. Missing data will be assumed MAR in the primary analysis. Missing data will be imputed in sensitivity analyses as described below in Section 7.1.3.

7.1.3. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 9: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints defined in Section 7.1 will be summarized using descriptive statistics, graphically presented and listed.

An overall forest plot will be produced for each ITT population showing the adjusted treatment differences with corresponding 95% confidences intervals for the primary, secondary and other efficacy endpoints.

The amount of missing data for the primary endpoint of AM PEF will also be summarized for the ITT (5-11 Years Old) Population. This summary will include the number of non-missing daily AM PEF values available to be used in the endpoint out of the possible 84; and also, the percentage of non-missing daily AM PEF values between the first and last non-missing day.

7.1.3.1. Statistical Methodology Specification

Primary Endpoint – ITT (5-17 Years Old) Population
• Weighted mean FEV_1 (0-4 hours) (L) at Week 12
Primary Endpoint – ITT (5-11 Years Old) Population
• Change from baseline in AM PEF (L/min) over Weeks 1-12
Model Specification
• Statistical analyses will be performed with analysis of covariance (ANCOVA) models with effects due to baseline, region, sex, age and treatment group. • Two models will be fitted; one with a response variable of weighted mean FEV_1, and one with a response variable of change from baseline in weighted mean FEV_1. Two models will be fitted in a similar manner for AM PEF. • Primary statistical analyses will include all available data, regardless of whether the participant remained on-treatment at the time of the assessment. • Missing data will be assumed to be missing at random (MAR). Sensitivity analyses to investigate the impact of this assumption will be conducted as described below. • A SAS procedure of the following structure will be used: proc mixed data=start ; class trtcd sex region ; model response_var = trtcd sex region age baseline / ddfm=kr s cl ; lsmeans trtcd / cl diff om ; ods output lsmeans=lsmeans ; ods output diffs=diffs ; run ; quit ;
Model Checking & Diagnostics
• The Kenward-Roger (KR) method (Kenward, 1997) 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 analyses. This will be achieved by specifying the DDFM=KR option in the MODEL statement within PROC MIXED. • For mixed model repeated measures (MMRM) models (specified for sensitivity and secondary efficacy analyses), an unstructured covariance structure for the R matrix will be used by specifying 'TYPE=UN' in the REPEATED statement. o In the event that this model fails to converge, then the residual method will be used instead. • Appropriate graphs will be reviewed as part of the model checking process to ensure that distributional assumptions hold. These will include a normal probability plot of the residuals and a plot of the residuals versus the fitted values (checking the normality assumption and constant

variance assumption of the model, respectively).

- Interactions with treatment will be explored for other model covariates and tests for interactions will be at the 2-sided 10% significance level. Any significant interactions that are found will be thoroughly investigated and where necessary, extra outputs will be produced.

Model Results Presentation

- The adjusted mean and adjusted mean change from baseline with corresponding standard error for each treatment group will be presented. The estimated treatment difference will be presented together with 95% confidence interval (CI) for the difference and p-value for the inequality comparison.

Sensitivity and Supplemental Analyses

Sensitivity Analysis – MMRM Analysis

- For the primary endpoint of AM PEF, a sensitivity analysis for the primary estimand will be performed including all data from Weeks 1-12 (regardless of treatment state). For this analysis, the Weeks 1-12 time period will be split into 6 separate time periods: Weeks 1-2, Weeks 3-4, Weeks 5-6, Weeks 7-8, Weeks 9-10 and Weeks 11-12. The mean change from baseline in AM PEF will then be analyzed using a MMRM model, which will allow for effects due to baseline AM PEF, region, sex, age, time period and treatment group. This model will also contain a time period-by-baseline interaction term and a time period-by-treatment interaction term. The 2-weekly means will be used in the MMRM analysis, however an average treatment effect and treatment comparison across Weeks 1-12 will be obtained. While missing data are not implicitly imputed in this analysis, there is an underlying assumption that the data are MAR. All non-missing data for a participant will be used within the analysis and, via modelling of the within-subject correlation structure, the derived treatment differences will be adjusted to take into account missing data.
- A SAS procedure of the following structure will be used:

```
proc mixed data=start ;
        class trtcd sex region week subjid ;
        model response_var = trtcd sex region age baseline
                                week week*baseline week*trtcd / ddfm=kr s cl ;
        repeated week / subject=subjid type=un ;
        lsmeans trtcd / cl diff e om=OMdset at (baseline age)=(&blm. &agem.) ;
        ods output lsmeans=lsmeans ;
        ods output diffs=diffs ;
run ;
quit ;
```

where OMdset is a dataset with a row for every 2-weekly interval-subject combination that contains all the covariates and blm and agem are macro variables containing the means for baseline and age for the participants in the analysis. These are used to derive the adjusted means using coefficients which are based on the participants in the analysis.

- For the average Weeks 1-12 analysis, the adjusted mean and adjusted mean change from baseline with corresponding standard error for each treatment and the estimated treatment difference will be presented together with a 95% CI for the difference and p-value for the inequality comparison.

Sensitivity Analyses – Multiple Imputation Methods
• Missing data sensitivity analyses using multiple imputation (MI) methods [as described below in Section 7.1.3.2 (Jump to Reference Method) and Section 7.1.3.3(Tipping Point Analysis)] will be conducted to investigate the impact of missing data and to examine the robustness of the analyses of the primary endpoints to departures from the assumption that missing data are MAR. • The MI methods are based on pattern-mixture models described by Carpenter (Carpenter, 2013). The pattern-mixture model approach to sensitivity analysis models the distribution of a response as the mixture of a distribution of the observed responses and a distribution of the missing responses. Missing values are then imputed under a plausible scenario for which the missing data are missing not at random (MNAR). Clinical judgment can then be applied as to the plausibility of the associated assumptions and any differences of inference under MAR. • The sensitivity analyses will be performed for the primary estimand including all data regardless of treatment state.
Supplemental Analyses Addressing a Different Estimand – Primary Endpoint
• A supplementary treatment effect to be estimated will be the hypothetical effect of no occurrence of the intercurrent event of treatment discontinuation (i.e., if all participants had stayed on their randomized treatment). This will address a mixed strategy estimand, whereby a hypothetical strategy is applied for the intercurrent event of treatment discontinuation and a treatment policy strategy is applied for the intercurrent event of rescue medication use (i.e. data used regardless of use of rescue medication). • To evaluate this supplementary estimand, the ANCOVA models for the primary efficacy endpoints will be rerun using only on-treatment data. • Data collected up to the time of treatment discontinuation will be used in the analysis. Data collected after treatment discontinuation will be set as missing. Missing data will be assumed to be MAR. • The model specification, model checking and diagnostics, and model results presentation will be the same as described for the primary analysis (including on- and post-treatment data).
Supplemental Analyses Addressing a Different Estimand – Serial FEV_1
• The individual serial FEV_1 assessments used to derive the weighted mean endpoint at Week 12 will each be analysed separately by their planned time (pre-dose and 30 minutes and 1, 2, 3 and 4 hours post-dose). • These analyses will each be performed using an ANCOVA model allowing for the effects due to baseline FEV_1, region, sex, age and treatment group. • The adjusted means and adjusted mean changes from baseline with corresponding standard error for each treatment group, estimated treatment differences and 95% CIs for the differences will be presented for each time point. The adjusted mean changes from baseline for each treatment will be plotted along with the corresponding 95% CIs. • These analyses will be performed for both ITT populations using on-treatment data.
Supplemental Analysis at Week 12 and Using Different Missing Data Handling – AM PEF
• For the endpoint of AM PEF, an additional analysis will be performed on the ITT (5-17 Years Old) population, which will assess change from baseline at Week 12 using an MMRM analysis. For this analysis, the Weeks 1-12 time period will be split into 12 separate 1 week time periods:

Week 1, Week 2, Week 3… Week 12.

- In addition, the analysis at Week 12 will be repeated using a different missing data threshold. The Weekly AM PEF values will be considered missing if less than 4 days in a given week are recorded in the time period of interest.
- The analysis will be performed with MMRM models which will allow for effects due to baseline AM PEF, region, sex, age, week and treatment group. The models will also contain a week -by-treatment interaction term and a week -by-baseline interaction term.
- Two models will be fitted; one with a response variable of AM PEF and one with a response variable of change from baseline in AM PEF.
- A SAS procedure of the following structure will be used:

```
proc mixed data=start ;
        class trtcd sex region week subjid ;
        model response_var = trtcd sex region age baseline
                                week week *baseline week *trtcd / ddfm=kr s cl ;
        repeated week / subject=subjid type=un ;
        lsmeans week *trtcd / cl diff e om=OMdset at (baseline age)=(&blm. &agem.) ;
        ods output lsmeans=lsmeans ;
        ods output diffs=diffs ;
run ;
quit ;
```

where OMdset is a dataset with a row for every week -subject combination that contains all of the covariates and blm and agem are macro variables containing the means for baseline and age for the participants in the analysis. These are used to derive the adjusted means using coefficients which are based on the participants in the analysis.

- The adjusted means and adjusted mean changes from baseline with corresponding standard error for each treatment group, estimated treatment differences and 95% CIs for the differences will be presented for each time point.
- These analyses will be performed for the ITT population using all available data (both on-treatment and post-treatment).

7.1.3.2. Jump to Reference Statistical Analyses of Weighted Mean FEV_1 (0-4 Hours) and AM PEF

Implementation of the jump to reference (J2R) method assumes that for participants in the experimental treatment group (FF/VI) with missing data, their imputed mean response is that of the reference treatment group (FF). The J2R method may be considered a 'worst case' scenario which is likely to give a conservative estimate of treatment effect because the missing data is assumed to follow the same 'reference pattern' in all participants regardless of their study treatment.

Within each treatment group a multivariate normal model will be fitted using a Markov Chain Monte Carlo (MCMC) approach so that independent samples of the model parameters [i.e., the estimated betas associated with treatment, sex, region, etc., and the estimated variance and covariance parameters can be taken (from the posterior distributions)]. For weighted mean FEV_1, the covariates will be the same as the primary ANCOVA model and for AM PEF, the covariates will be the same as for the repeated

measures sensitivity analysis. This approach allows all missing observations to be imputed, whether a participant has a non-monotone (under MAR) or monotone (under J2R) pattern of missing data.

The independent samples drawn from the posterior distributions for the mean and variance-covariance matrix provide input into the imputation model. For each participant with missing data, these sampled values of the parameters for mean vectors and the variance-covariance matrices specify a joint distribution for their observed and unobserved outcome data. Under the J2R approach, the mean estimate is constructed using the estimated beta associated with the reference treatment, as well as the participant's other covariates.

For each participant with missing data, this joint pattern-specific distribution can be used to construct the conditional distribution of their missing data given their observed data. The missing data is sampled once from this distribution to create a single dataset for each imputation. Together these form a series of complete imputed datasets for each of the primary endpoints (with imputed data in the reference arm under MAR and in the FF/VI arm under J2R).

Each imputation dataset will be analyzed using an ANCOVA model for weighted mean FEV_1 with the same covariates as the primary analysis model. For each AM PEF imputation dataset, a repeated measures analysis will be carried out using the two-week means (Weeks 1-2, 3-4, 5-6, 7-8, 9-10 and 11-12) data, using the same covariates as in the repeated measures average over Weeks 1-12 sensitivity analysis and obtaining the average treatment effect and treatment comparison across Weeks 1-12. For both endpoints, the results from each analysis of each sample will then be combined using Rubin's method (Rubin, 1987) as implemented in PROC MIANALYZE in SAS. The seeds for all planned MI analyses will be defined and documented prior to unblinding the database.

Sensitivity Statistical Analyses – Jump to Reference Multiple Imputation Method
Primary Endpoint – ITT (5-17 Years Old) Population
• Weighted mean FEV_1 (0-4 hours) at Week 12 (including imputed data)
Primary Endpoint – ITT (5-11 Years Old) Population
• Change from baseline in AM PEF (L/min) Averaged over Weeks 1-12 (including imputed data)
Model Specification and Results Presentation
• ANCOVA model with the same covariates as the primary analysis model will be used for weighted mean FEV_1. • MMRM model with the same covariates as in the repeated measures average over Weeks 1-12 sensitivity analysis will be used for AM PEF. • Results presentation will be the same as for the primary analysis of weighted mean FEV_1 and MMRM analysis of AM PEF as described in Section 7.1.3 Statistical Analyses / Methods.

7.1.3.3. Tipping Point Statistical Analysis of Weighted Mean FEV_1 (0-4 Hours)

A tipping point sensitivity analysis will be conducted under a range of missing data assumptions to determine how extreme these assumptions need to be for the conclusion

of the primary analysis to change, (i.e., under which there is no longer evidence of a treatment effect). Assumptions about missing weighted mean FEV_1 values at Week 12 on the FF/VI arm and the FF arm will vary independently, and will include scenarios where participants with missing data in the FF/VI treatment group have worse outcomes than participants with missing data in the FF treatment group. This analysis will allow for determination of the 'tipping point(s)', the mean values for missing data that would cause a change in the statistical significance of the result of the treatment comparison.

For each treatment group, the imputed weighted mean FEV_1 values will vary separately by a value of delta, where delta represents the value of weighted mean FEV_1 at Week 12. Based on the research article written by Permutt [Permutt, 2015], the deltas investigated for each treatment group will cover a range greater than the expected treatment difference under the MAR assumption. Specifically, the deltas for both the FF/VI and FF treatment groups will each independently range from -0.120 L to 0 L, in 0.020 L increments.

Multiple implementation methods will be used to complete the data record for participants with missing data. For each imputation, a random draw will be made from a normal distribution with mean equal to the corresponding assumed value, and standard deviation taken from observed data. Weighted mean FEV_1 values will be imputed for each value of delta and for each completed imputation data set an ANCOVA will be carried out. The analysis model will allow for effects due to baseline FEV_1, region, sex, age and treatment group. Treatment effects and differences will be estimated and then combined across imputations using standard MI rules and Rubin's method (Rubin, 1987) as implemented in PROC MIANALYZE in SAS. The seeds for all planned MI analyses will be defined and documented prior to unblinding the database.

Sensitivity Statistical Analysis – Tipping Point Multiple Imputation Method
Primary Endpoint – ITT (5-17 Years Old) Population
• Weighted mean FEV_1 (0-4 hours) (L) at Week 12 (including imputed data)
Model Specification and Model Results Presentation
• ANCOVA model with the same covariates as the primary analysis model will be used. • The adjusted means with corresponding standard errors for each treatment group will be presented with the treatment differences, associated 95% CIs and p-values for each treatment comparison made across the range of imputed values. • A cross-tabulation of p-values will also be provided for each treatment comparison made across the range of imputed values.

7.2. Secondary Efficacy Analyses

7.2.1. Endpoints

ITT (5-17 Years Old) Population

- Change from baseline in AM PEF (L/min) over Weeks 1-12

ITT (5-11 Years Old) Population

- Weighted mean FEV_1 (0-4 hours) (L) at Week 12

Both ITT (5-17 Years Old) and ITT (5-11 Years Old) Populations

- Change from baseline in the percentage of rescue-free 24-hour periods over Weeks 1-12
- Change from baseline in the percentage of symptom-free 24-hour periods over Weeks 1-12
- Change from baseline in morning FEV_1 (L) at Week 12
- Change from baseline in ACQ-5 at Week 24
- Incidence of exacerbations over Weeks 1-24

7.2.2. Summary Measure

For all secondary endpoints other than asthma exacerbations, the summary measure of interest is the adjusted mean treatment difference. The incidence of exacerbations will be summarized.

7.2.3. Strategy for Intercurrent (Post-Randomization) Events

The primary treatment effect to be estimated is the treatment policy effect of initial randomized treatment. Intercurrent events considered to have an impact on estimation of the treatment effect are:

- Discontinuation of randomized treatment
- Increased use of rescue medication
- Withdrawal from the study

All recorded data up to the time of study withdrawal will be included in the analyses of the secondary endpoints, regardless of discontinuation of randomized treatment or increased use of rescue medication. To minimize study withdrawals, participants who discontinue randomized treatment will be encouraged to stay in the study and complete all remaining protocol-specified visits.

Missing data will be assumed MAR in the secondary efficacy analyses. Missing data will be imputed in sensitivity analyses of the secondary endpoints as described below in Section 7.2.4.1.

7.2.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 9: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints defined in Section 7.2.1 will be summarized using descriptive statistics and graphically presented.

The amount of missing data for the powered secondary efficacy endpoint of change from baseline in percentage of rescue-free 24-hour periods for the ITT (5-11 Years Old) Population will also be summarized. This summary will include the number of non-missing 24-hour periods available to be used in the endpoint out of the possible 84; and also, the percentage of non-missing 24-hour periods between the first and last non-missing 24-hour period.

7.2.4.1. Statistical Methodology Specification

The secondary endpoints of AM PEF for the ITT (5-17 Years) Population and weighted mean FEV_1 (0-4 hours) for the ITT (5-11 Years) Population will be analyzed as described for the primary analyses of these endpoints in Section 7.1 Primary Efficacy Analyses. These analyses will include the MMRM and J2R sensitivity analyses as described in Section 7.1.3.

Endpoints

- Change from baseline in the percentage of rescue-free 24-hour periods over Weeks 1-12
- Change from baseline in the percentage of symptom-free 24-hour periods over Weeks 1-12

Model Specification

- Statistical analyses will be performed with ANCOVA models with effects due to baseline, region, sex, age and treatment group.
- The statistical analyses will include all available data, regardless of whether the participant remained on-treatment at the time of the assessment.
- A SAS procedure of the following structure will be used:

```
proc mixed data=start ;
        class trtcd sex region ;
        model response_var = trtcd sex region age baseline / ddfm=kr s cl ;
        lsmeans trtcd / cl diff om ;
        ods output lsmeans=lsmeans ;
        ods output diffs=diffs ;
run ;
quit ;
```

Model Checking & Diagnostics

- Refer to Section 7.1.3.1 Statistical Methodology Specification.
- If the distributional assumption of normality fails then an additional statistical analysis will be performed on categorized data using proportional odds. The percentage of rescue-free/symptom-free 24-hour periods will be calculated for each participant and assigned to one of the following 4 categories: 0-<25, 25-<50, 50-<75 and 75-100. The categorized data will then be analyzed using logistic (proportional odds) regression with the same covariates as given above for the ANCOVA model. The estimated treatment differences will be displayed as odds ratios together with 95% CIs and p-values for the treatment comparisons. The decision to do this additional analysis will be taken separately for each endpoint and population.

Model Results Presentation

- The adjusted mean change from baseline with corresponding standard error for each treatment group will be presented. The estimated treatment difference will be presented together with the corresponding 95% CI for the difference and p-value for the inequality comparison.
- The adjusted mean change for each treatment group and the estimated treatment difference will also be converted into the equivalent number of additional rescue-free/symptom-free days per week and these will also be presented along with the original percentages. The conversion is achieved by taking the original value which is expressed as a percentage and dividing by 100 then multiplying by 7.

Sensitivity and Supplemental Analyses
Sensitivity Analyses – MMRM Analyses
• For both endpoints and ITT populations, sensitivity analyses for the primary estimand will be performed including all data from Weeks 1-12 (regardless of treatment state). For these analyses, the Weeks 1-12 time period will be split into 6 separate time periods: Weeks 1-2, Weeks 3-4, Weeks 5-6, Weeks 7-8, Weeks 9-10 and Weeks 11-12. These 2-weekly means will be used in the MMRM analysis of mean change from baseline in percentage of rescue-free (and symptom-free) 24-hour periods, however an average treatment effect and treatment comparison across Weeks 1-12 will be obtained. The model specification, model checking and diagnostics, and model results presentation will be the same as described for the MMRM sensitivity analysis of mean change from baseline in AM PEF in Section 7.1.3.1.
Sensitivity Analyses – Multiple Imputation Methods
• For both endpoints and ITT populations, missing data sensitivity analyses using J2R MI methods (as described in Section 7.1.3.2 for AM PEF) will be conducted to investigate the impact of missing data and to examine the robustness of the analyses to departures from the assumption that missing data are MAR.
Supplemental Analysis Addressing a Different Estimand
• A supplementary treatment effect to be estimated will be the hypothetical effect of no occurrence of the intercurrent event of treatment discontinuation (i.e., if all participants had stayed on their randomized treatment). This will address a mixed strategy estimand, whereby a hypothetical strategy is applied for the intercurrent event of treatment discontinuation and a treatment policy strategy is applied for the intercurrent event of rescue medication use (i.e. data used regardless of use of rescue medication). • To evaluate this supplementary estimand, the ANCOVA model will be repeated using only on-treatment data for the powered secondary efficacy endpoint of change from baseline in percentage of rescue-free 24-hour periods for the ITT (5-11 Years Old) Population. • Data collected up to the time of treatment discontinuation will be used in the analysis. Data collected after treatment discontinuation will be set as missing. Missing data will be assumed to be MAR. • The model specification, model checking and diagnostics, and model results presentation will be the same as described for the primary analysis (including on- and post-treatment data).

Endpoints
• Change from baseline in morning pre-dose FEV_1 (L) at Week 12 • Change from baseline in ACQ-5 at Week 24
Model Specification
• Statistical analyses will be performed with MMRM models which will allow for effects due to baseline (FEV_1 or ACQ-5 score), region, sex, age, visit and treatment group. The models will also contain a visit-by-treatment interaction term and a visit-by-baseline interaction term. • Two models will be fitted; one with a response variable of pre-dose FEV_1 and one with a response variable of change from baseline in pre-dose FEV_1. Two models will be fitted in a similar manner for the ACQ-5.

- For FEV_1, the pre-dose measurements from scheduled Visits 4, 5 and 6 (Weeks 4, 8 and 12) will be included in the models.
- For ACQ-5, the scores from scheduled Visits 6 and 9 (Weeks 12 and 24) will be included in the models.
- The statistical analyses will include all available data, regardless of whether the participant remained on-treatment at the time of the assessment.
- A SAS procedure of the following structure will be used:

```
proc mixed data=start ;
        class trtcd sex region visit subjid ;
        model response_var = trtcd sex region age baseline
                                visit visit*baseline visit*trtcd / ddfm=kr s cl ;
        repeated visit / subject=subjid type=un ;
        lsmeans visit*trtcd / cl diff e om=OMdset at (baseline age)=(&blm. &agem.) ;
        ods output lsmeans=lsmeans ;
        ods output diffs=diffs ;
run ;
quit ;
```

where OMdset is a dataset with a row for every visit-subject combination that contains all of the covariates and blm and agem are macro variables containing the means for baseline and age for the participants in the analysis. These are used to derive the adjusted means using coefficients which are based on the participants in the analysis.

Model Checking & Diagnostics

- Refer to Section 7.1.3.1 Statistical Methodology Specification.

Model Results Presentation

- The adjusted means and adjusted mean changes from baseline with corresponding standard errors for each treatment group will be presented. The estimated treatment differences will be presented together with 95% CIs for the differences and p-values for the inequality comparisons.

Sensitivity Analyses – Multiple Imputation Methods

- For both endpoints and ITT populations, missing data sensitivity analyses using J2R MI methods (as described in Section 7.1.3.2 for AM PEF) will be conducted. Each imputed data set will be analyzed at the final visit using a univariate version of the model used for the primary analysis.
- The Week 12 morning FEV_1 data from each sample will be analyzed using an ANCOVA model using the same covariates as the original model of FEV_1 (with the exception of the visit covariate and its interactions).
- The Week 24 ACQ-5 score data from each sample will be analyzed using an ANCOVA model using the same covariates as the original model of ACQ-5 (with the exception of the visit covariate and its interactions).
- The results from the analyses of each sample for FEV_1 and of each sample for ACQ-5 will be combined, respectively, using Rubin's method as implemented in PROC MIANALYZE in SAS.
- Results presentation will be similar to the primary analysis (ANCOVA) described in Section 7.1.3 Statistical Analyses / Methods.

Endpoint
• Incidence of asthma exacerbations
Summary

• The number and percentage of participants reporting an asthma exacerbation (on-treatment and post-treatment) will be summarized by treatment group.
• The number and percentage of participants with each number of exacerbations (0, 1, 2, 3, 4, >4) and the total number of exacerbations per treatment group will also be summarized.
• The number and percentage of participants with an exacerbation that led to withdrawal of blinded study drug, hospitalization, systemic/oral corticosteroids being taken, intubation, or emergency room visit will be summarized by treatment group.
• The number and percentage of participants by frequency of healthcare contacts (0, 1, 2, 3, 4, >4) will be summarized by contact type and treatment group to characterize the level of healthcare associated with an asthma exacerbation. The frequency counts for each participant will be the total sum of contacts (or days in hospital) by type.
• The following types of healthcare contact for an exacerbation are recorded in the eCRF:
  • Number of telephone calls
  • Number of home/day visits
  • Number of home/night visits
  • Number of office/practice visits
  • Number of urgent care/outpatient visits
  • Number of emergency room visits
  • Number of days in intensive care
  • Number of days in general ward

7.3. Other Efficacy Analyses

One other efficacy endpoint defined for both the ITT (5-17 Years) Population and the ITT (5-11 Years) Population is change from baseline in PM PEF (L/min) over Weeks 1-12. PM PEF will be analyzed in the same manner as the primary analysis of AM PEF, using all available data from Weeks 1-12 regardless of whether the participant remained on-treatment at the time of the measurement. These analyses will include the MMRM and J2R MI sensitivity analyses as described in Section 7.1.3 for AM PEF.

8. SAFETY ANALYSES

Safety analyses will be based on the ITT (5-17 Years Old) Population and the ITT (5-11 Years Old) Population and will include all study data (both on-treatment and post-treatment), unless otherwise specified.

8.1. Adverse Events Analyses

Adverse events summaries including summaries of AEs, serious adverse events (SAEs) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 9: List of Data Displays.

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) coding dictionary. The version of MedDRA used in reporting will be noted in a footnote of the AE overview table.

For the standard on-treatment and post-treatment AE tables, the number and percentage of participants with all AEs (regardless of causality) will be summarized for each treatment group by system organ class (SOC) and preferred term (PT). The ordering of the SOCs and the PTs within the SOCs will both be in descending order of total incidence. A SOC will not be presented when the overall incidence for any AE within the particular system is zero. If the total incidence for any two or more AEs is equal, the events will be presented in alphabetical order.

Number, percentage and incidence rate (per 100 person years) of participants with any AEs/SAEs will be summarized for each treatment group for every COVID-19 pandemic period (pre, during, post-pandemic).

8.2. Adverse Events of Special Interest Analyses

A comprehensive list of MedDRA terms based on clinical and safety review will be used to identify AEs of special interest to FF and FF/VI. Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting and/or emerging data from on-going studies may highlight additional AEs 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 clinical and safety review agreements documented and in place at time of reporting and prior to unblinding the study. The details of the planned displays are provided in Appendix 9: List of Data Displays.

The number and percentage of participants with AEs of special interest will be summarized for each treatment group by special interest term, subgroup and PT. The ordering of the special interest terms, the subgroups and the PTs within them will all be in descending order of total incidence. If the total incidence for any two or more AEs is equal, the events will be presented in alphabetical order. This summary will include both on-treatment and post-treatment AEs. This summary will be repeated for on-treatment and post-treatment SAEs.

8.3. Fasting Glucose

Fasting glucose will be collected at Screening (Visit 1) and Week 24 (Visit 9), or at the Early Treatment Discontinuation Visit or Early Withdrawal Visit if applicable. Summary statistics of fasting glucose values and change from baseline values will be presented. Fasting glucose change from baseline at Week 24 will also be analyzed using an ANCOVA model with effects due to baseline, region, sex, age and treatment group. Two models will be fitted; one with a response variable of fasting glucose, and one with a response variable of change from baseline. The adjusted means and adjusted mean changes from baseline with corresponding standard errors for each treatment group and the estimated treatment difference for the treatment comparison will be presented together with the corresponding 95% CI and p-value. This analysis will be repeated to include the maximum change from baseline value for each participant (from an unscheduled visit, Week 24 Visit, Early Treatment Discontinuation Visit or Early Withdrawal Visit).

8.4. ECGs and Vital Signs

12-lead ECG measurements will be performed at Screening (Visit 1) and Week 24 (Visit 9), or at the Early Treatment Discontinuation Visit or Early Withdrawal Visit if applicable. Vital signs (systolic and diastolic blood pressure and heart rate) will be collected at Screening.

The summaries of ECGs and vital signs will be based on GSK Core Data Standards and the details of the planned displays are presented in Appendix 9: List of Data Displays. For the displays of ECG findings of potential clinical importance, a list of ECG findings considered to be of potential clinical importance will be documented prior to unblinding the study.

In addition to the core standard displays of ECG values and change from baseline values, the QTc(F), QTc(B) and heart rate change from baseline values at Week 24 will also be analyzed using ANCOVA models with effects due to baseline, region, sex, age and treatment group. Two models will be fitted; one with a response variable of the ECG value, and one with a response variable of change from baseline. The adjusted means and adjusted mean changes from baseline with corresponding standard errors for each treatment group and the estimated treatment differences for the treatment comparisons will be presented together with the corresponding 95% CIs and p-values. These analyses will be repeated to include the maximum change from baseline values for each participant (from an unscheduled visit, Week 24 Visit, Early Treatment Discontinuation Visit or Early Withdrawal Visit).

Additionally, QTc(F), QTc(B), change from baseline in QTc(F) and change from baseline in QTc(B) will be categorized and summarized by treatment group in frequency tables.

8.5. Oropharyngeal Examination

Oropharyngeal examinations will be conducted at Screening (Visit 1), Randomization (Visit 3) and Week 24 (Visit 9), or at the Early Treatment Discontinuation Visit or Early

Study Withdrawal Visit if applicable. Any adverse finding will be recorded as an AE or SAE and included in summaries and listings of AEs/SAEs.

8.6. Pregnancy

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.

8.7. Other Safety Measures

All investigational product (IP) inhaler malfunction data for participants reporting at least one IP inhaler malfunction will be listed. All pneumonia data collected on the pneumonia eCRF page will be listed. For any deaths, cardiovascular events or liver events reported during the study, Integrated Data Standards Library (IDSL) standards for reporting will be followed for all data collected in the eCRF.

A summary of risks plot will be produced summarizing the following AE information:

- SAE (any)
- Withdrawal due to AE (including events leading to permanent discontinuation of study drug and/or withdrawal from the study)
- AESI (any)

Individual AESI will also be summarized:

- Pneumonia
- Local steroid effects
- Effects on glucose
- Hypersensitivity
- Tremor
- Cardiovascular effects

The frequencies, relative risks and corresponding 95% CIs for the FF/VI versus FF treatment groups will be displayed for both ITT populations. Calculations of the relative risks and 95% CIs are described in Appendix 6: Derived and Transformed Data.

9. REFERENCES

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10. APPENDICES

10.1. Appendix 1: Protocol Deviation Management

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the PDMP. Important protocol deviations occurring during study conduct as identified in the PDMP and determined by the study team will be summarized and listed. The following protocol deviations have been defined in this study.

Number	Protocol Deviation(s) Description
01	Participant signature and/or date are missing from the Informed Consent document.
02	Study specific procedure performed before Informed Consent was signed.
03	Failure of inclusion criteria 1-9, exclusion criteria 1-17, randomization inclusion criteria 1-5, or randomization exclusion criteria 1-5 as described in Section 6 of the protocol [GlaxoSmithKline Document Number 2016N298634_00].
04	Participant becomes pregnant but is not withdrawn from study treatment.
05	Female participant who reaches menarche after Visit 1 and does not agree to follow the contraception guidance as described in Appendix 5 of the protocol [GSK Document Number 2016N298634_00], but is not withdrawn from study treatment.
06	Participant meets the liver stopping criteria but is not withdrawn from study treatment.
07	Participant meets the QTc stopping criteria but is not withdrawn from study treatment.
08	Participant withdrew from the study and requested destruction of any samples (e.g. saliva) taken and not tested, and not documented in the site study records.
09	Serious adverse event (SAE) relationship was not assessed within 72 hours.
10	SAE was not reported within 24 hours.
11	Genetic Research Sample was not destroyed after withdrawal of consent.
12	Genetic Research Sample was obtained without consent.
13	Study Visit (1-10) occurred outside of allowed window period.
14	Study Visit 8 is missing and no telephone call was performed.
15	Early Treatment Discontinuation Visit was not conducted within approximately 24 hours of the participant stopping study medication.
16	Study visit was not done and participant was still on study treatment.
17	Study treatment was restarted/re-challenged after liver chemistry stopping criteria met.
18	Study treatment restarted after participant withdrew from treatment.
19	Study treatment restarted after participant withdrew from the study.
20	Accidental unblinding occurred.
21	Study treatment was misallocated (incorrect treatment known at unblinding).
22	Short-acting beta agonist (SABA) use was not withheld for 4 hours prior to the FEV_1 measurement.
23	Oropharyngeal exam was not performed at required timepoint.
24	Serial spirometry was not performed at required timepoint.
25	Pre-dose FEV_1 measurement was not performed between 6-11 a.m.
26	Study drug was not withheld prior to coming to the clinic and performing the FEV_1 measurement.
27	Incorrect run-in medication dispensed.

10.2. Appendix 2: Schedule of Activities

10.2.1. Protocol Defined Schedule of Events

Procedure	Screening	Pre-randomisation	Randomisation	Treatment Period (Days, Weeks)						ETD	EW	FU TC (7 days post-last visit)
Visit	**V1[1]**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**			**V10**
Week	**-4 to Day 0**		**0**	**4**	**8**	**12**	**16[2]**	**20[3]**	**24**			**25**
Day (All visits except V2 to occur within -5 to +2 days of specified day)	**-28**	**-5 (-2 to +2)**	**0**	**28**	**56**	**84**	**112**	**140**	**168**			**175**
Informed consent and assent	X											
Pharmacogenetics consent and assent	←==========		==========→									
Inclusion and exclusion criteria	X											
Randomisation criteria			X									
Demography	X											
Medical history	X											
Asthma history	X											
Exacerbation history	X											
Full physical exam including, height and weight	X											
EFFICACY ASSESSMENTS												
Electronic patient diary [4]	←==========					==========→				X	X	
FEV_1	X	X		X	X	X				X	X[5]	
FEV_1 review of the overread only			X									
Serial FEV_1						X						
Lung function (FEV_1) reversibility testing[6]	X											
cACT/ACT	X		X									

Procedure	Screening	Pre-randomisation	Randomisation	Treatment Period (Days, Weeks)						ETD	EW	FU TC (7 days post-last visit)
Visit	**V1[1]**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**			**V10**
Week	**-4 to Day 0**		**0**	**4**	**8**	**12**	**16[2]**	**20[3]**	**24**			**25**
Day (All visits except V2 to occur within -5 to +2 days of specified day)	**-28**	**-5 (-2 to +2)**	**0**	**28**	**56**	**84**	**112**	**140**	**168**			**175**
ACQ			X			X			X			
SAFETY ASSESSMENTS												
Oropharyngeal examination	X		X						X	X	X[7]	
Concomitant medication review	X		←==========	==========	==========	==========	==========	==========	==========→	X	X	X
12-lead ECG	X								X	X	X[8]	
Vital signs	X											
AE review			←==========	==========	==========	==========	==========	==========	==========→	X	X	X
SAE review	X		←==========	==========	==========	==========	==========	==========	==========→	X	X	X
Exacerbation review			←==========	==========	==========	==========	==========	==========	==========→	X	X	X
LABORATORY ASSESSMENTS												
Blood draw for fasting glucose[9]	X								X	X	X[10]	
Pregnancy Test	X								X	X	X	
Pharmacogenetic sample (saliva)[11]				X								
STUDY TREATMENT												
Dispense standardised FP run-in medication	X											
Return FP run-in medication			X									
Dispense SABA rescue inhaler	X											

Procedure	Screening	Pre-randomisation	Randomisation	Treatment Period (Days, Weeks)						ETD	EW	FU TC (7 days post-last visit)
Visit	**V1[1]**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**			**V10**
Week	**-4 to Day 0**		**0**	**4**	**8**	**12**	**16[2]**	**20[3]**	**24**			**25**
Day (All visits except V2 to occur within -5 to +2 days of specified day)	**-28**	**-5 (-2 to +2)**	**0**	**28**	**56**	**84**	**112**	**140**	**168**			**175**
Return SABA rescue inhaler									X		X	
Treatment assignment (randomisation) via IVRS			X									
Dispense double-blind study treatment via IVRS/IWRS			X	X	X	X	X[12]	X				
Return double-blind study treatment				X	X	X	X	X	X	X	X	

Abbreviations: AE=adverse event; ACT=Asthma control test; cACT=Childhood asthma control test; ACQ=Asthma Control Questionnaire; ECG=electrocardiogram; ETD=early treatment discontinuation; EW=early withdrawal; FEV_1=forced expiratory volume in 1 second; FP=fluticasone propionate; FU=follow-up; IVRS=interactive Voice Response System/Interactive Web Response System; SABA= short-acting beta agonist; SAE=serious adverse event; TC=telephone call; V=Visit.

1. Prior to any study activities at Visit 1, including fasting for the blood glucose test, written informed consent should be obtained from at least one 1 parent/care giver (legal guardian) and accompanying informed assent from the participant (where the participant is able to provide assent).
2. Week 16 (Visit 7) can be parent only visit.
3. Week 20 (Visit 8) can be a telephone call if there are no problems with compliance.
4. Asthma symptom scores, peak expiratory flow (PEF), rescue albuterol/salbutamol usage will be recorded on the electronic patient diary. To be completed every day in the morning and evening from Visit 1 through to Visit 6 only.
5. FEV_1 is not required at the Early Withdrawal Visit or Early Treatment Discontinuation Visit if these visits occurred after Visit 6.
6. Following administration of 2 to 4 inhalations of albuterol/salbutamol. Reversibility testing includes a baseline spirometry and repeat spirometry within 10 to 40 minutes after inhalation of 400 µg of salbutamol. The reversibility test will be considered positive if participants show improvement of FEV1 ≥12% after administration of salbutamol.
7. Oropharygneal examination is not required at the Early Withdrawal Visit if examination was performed at Early Treatment Discontinuation Visit.
8. A 12-lead ECG is not required at the Early Withdrawal Visit if it was measured at the Early Treatment Discontinuation Visit.
9. A blood draw is not required at the Early Withdrawal Visit if it was collected at the Early Treatment Discontinuation Visit.
10. A central laboratory will be used.
11. Informed consent for optional substudies, e.g. genetics consent must be obtained before collecting a sample. Sample to be obtained post-randomisation.
12. Two inhalers to be dispensed at Visit 7 as Visit 8 can be a telephone call only visit if there are no problems with compliance.

10.3. Appendix 3: Assessment Windows

10.3.1. General

Clinic visits are scheduled to take place as specified in Appendix 2: Schedule of Activities. Individual measurements will be reported based on the visits they are assigned to in the study database without adjustment. Measurements outside visit windows will not be excluded from analyses.

If a circumstance should arise where multiple measurements have been collected and recorded against the same timepoint, then the first valid value will be used for that timepoint.

10.3.2. Daily Diary

Participants are to complete a daily diary assessment each morning (prior to taking blinded study medication and rescue medication) and each evening. Participants are instructed to record the number of puffs of rescue albuterol used for relief of asthma symptoms and asthma symptom scores (over the past 12 hours), as well as PEF measurements each morning and evening.

Table 1 below displays which daily diary records are summarized for each analysis time period. Any diary data collected post the 12-week time period will not be included in the Weeks 1-12 analyses of diary data.

Table 1 Daily Diary Assessment Windows

Analysis for AM Measures		Analysis Window for PM Measures		Analysis Time Period
Beginning Timepoint (Day)	Ending Timepoint (Day)	Beginning Timepoint (Day)	Ending Timepoint (Day)	
-6	1	-7	-1	Baseline
2	85	1	84	Weeks 1 – 12
2	15	1	14	Weeks 1 - 2
16	29	15	28	Weeks 3 - 4
30	43	29	42	Week 5 - 6
44	57	43	56	Weeks 7 - 8
58	71	57	70	Weeks 9 - 10
72	85	71	84	Weeks 11 - 12
2	8	1	7	Week 1
9	15	8	14	Week 2

Note: There is no Day 0 in CDISC reporting. Days -7 to -1 are immediately pre-randomization and Day 1 is the day of randomization.

Note: Weeks 3 to 12 will be derived in a way consistent with the derivation shown for Weeks 1 and 2.

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

10.4.1. Study Phases

Assessments and events will be classified according to time of occurrence relative to the start and/or stop date of double-blind treatment. The earliest and latest exposure 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 or not, it will be considered as on-treatment.

10.4.1.1. Study Phases for Concomitant Medication

A medication will be summarized in every study phase (pre-, on- or post-treatment) in which it was taken, so a medication that was started during the run-in period and stopped during the double-blind treatment period will appear in both the pre-treatment and the on-treatment summaries.

On-treatment will be considered to be from the day after the double-blind treatment start date until the double-blind treatment stop date. Post-treatment will be considered to be from the day after the double-blind treatment stop date and onward. Pre-treatment will be considered prior to and until the day of double-blind treatment start.

10.4.1.2. Study Phases for Weighted Mean FEV_1 (0-4 hours)

Study Phase	Definition
On-Treatment	• Treatment Start Date ≤ Date of Measurement ≤ Treatment Stop Date
Post-Treatment	• Date of Measurement > Treatment Stop Date

10.4.1.3. Study Phases for AM Pre-dose FEV_1 and ACQ-5

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

10.4.1.4. Study Phases for Diary Efficacy Endpoints

Study Phase	Definition
Morning Measurement	
Pre-Treatment	• Date of Measurement ≤ Treatment Start Date
On-Treatment	• Treatment Start Date < Date of Measurement ≤ Treatment Stop Date + 1
Post-Treatment	• Date of Measurement > Treatment Stop Date + 1
Evening Measurement	
Pre-Treatment	• Date of Measurement < Treatment Start Date
On-Treatment	• Treatment Start Date ≤ Date of Measurement ≤ Treatment Stop Date
Post-Treatment	• Date of Measurement > Treatment Stop Date

Note: Participants are to record morning diary assessments prior to study drug administration so those on Treatment Start Date are prior to the first dose of study drug.

10.4.1.5. Study Phases for Asthma Exacerbations

Study Phase	Definition
Pre-Treatment	• Exacerbation Onset Date ≤ Treatment Start Date - 1
On-Treatment	• Treatment Start Date ≤ Exacerbation Onset Date ≤ Treatment Stop Date + 1
Post-Treatment	• Exacerbation Onset Date ≥ Treatment Stop Date + 2

Note: Asthma exacerbations are an efficacy endpoint in this study but treatment states are defined in the same manner as adverse events.

10.4.1.6. Treatment Emergent Flag for Adverse Events

Study Phase	Definition
Pre-Treatment	• AE Start Date ≤ Treatment Start Date – 1
On-Treatment	• Treatment Start Date ≤ AE Start Date ≤ Treatment Stop Date + 1
Post-Treatment	• AE Start Date ≥ Treatment Stop Date + 2
Onset Time Since First Dose (days)	Time Since First Dose will be derived as followed: • If Treatment Start Date or AE Onset Date are missing => missing • If Treatment Start Date > AE Onset Date then => AE Onset Date – Treatment Start Date • If Treatment Start Date ≤ AE Onset Date then => AE Onset Date – Treatment Start Date + 1

10.5. Appendix 5: Data Display Standards & Handling Conventions

10.5.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: uk1salx00175
HARP Compound	: arenv/arprod/gw685698_gw642444/hza107116
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards current to GSK reporting (Study Data Tabulation Model (SDTM) Implementation Guide Version 3.2 or higher and Analysis Data Model (ADaM) Implementation Guide Version 1.0 or higher).	
Generation of RTF Files	
• Rich Text Format (RTF) files will be generated for use in writing the CSR.	

10.5.2. Reporting Standards

General

- The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated:
  - 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

- All data will be reported according to the treatment the participant was randomized to unless otherwise stated.
- Numeric data will be reported (in listings) at the precision collected in the eCRF or recorded in the raw dataset if from non-eCRF sources.
- For summaries and analyses of variables other than FEV_1 and FVC (including FEV_1 percent predicted, FEV_1 percent reversibility, absolute FEV_1 reversibility (mL), FEV_1/FVC, derived diary endpoints and ACQ-5 score), the decimal places shown below for descriptive statistics and statistical analyses will be applied in the data displays.
- For summaries and analyses of FEV_1, FVC and weighted mean FEV_1 (L), the following number of decimal places will be applied:
  - Mean, Mean Change, Median, Least Squares (LS) Mean, LS Mean Change, Treatment Difference and 95% CI - report to 3 decimal places
  - SD, Std Err – report to 4 decimal places
  - Min, Max – report to 2 decimal places

Specification of Number of Decimal Places for Descriptive Statistics		
Label	**Description**	**Number of decimal places (dp) more than raw data**
N	Number of participants in the treatment group	Always present to 0 dp
n	Number of participants with non-missing values	Always present to 0 dp
Mean	Arithmetic Mean	1 dp
SD	Standard Deviation	2 dp
Median	Median	1 dp
Min.	Minimum	0 dp
Max.	Maximum	0 dp
Specification of Number of Decimal Places for Statistical Analysis		
Label	**Description**	**Number of decimal places (dp) more than raw data**
LS Mean	Adjusted mean for the treatment group	1 dp
LS Mean Change	Adjusted mean change from baseline for the treatment group	1 dp
Std Err	Standard error	2 dp
Difference	Treatment difference	1 dp
Odds Ratio	Treatment odds ratio	Always present to 2 dp
Relative Risk	Treatment relative risk	Always present to 2 dp
95% CI	95% Confidence interval around difference/ratio/relative risk	Same number of dp as the difference/ratio/relative risk
p-value	p-value	Always present to 3 dp (or <0.001 or >0.999)

Planned and Actual Time

- Reporting for tables, figures and formal statistical analyses:
  - Planned time relative to study drug dosing will be used in summaries, figures, statistical analyses and calculation of any derived parameters, unless otherwise stated.
- Reporting for data listings:
  - Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1).
  - Unscheduled or unplanned measurements will be presented within the data listings.

Unscheduled Visits

- Unscheduled visits will not be included in summary tables or figures.
- All unscheduled visits will be included in listings.

Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1.
Categorical Data	N, n, frequency, %

Graphical Displays

- Refer to IDSL Statistical 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. This will include all LS means, standard errors, treatment differences or ratios and confidence intervals. This will be done for all analysis tables regardless of whether or not a figure is planned as part of SAC.

- The programs for all graphical displays will additionally create a CSV file with the final data that is used in the graph in order to allow the graph to be redrawn for any potential future publication requirement.

10.6. Appendix 6: Derived and Transformed Data

10.6.1. General

Change from Baseline
• Calculated as the difference between the value of the endpoint at the timepoint of interest and the baseline value as defined in Section 5.2 Baseline Definitions
Time Since First Dose

• Calculated as the number of days from first dose date of double-blind treatment:
  • Ref Date = Missing → Time Since First Dose = Missing
  • Ref Date < First Dose Date → Time Since First Dose = Ref Date – First Dose Date
  • Ref Date ≥ First Dose Date → Time Since First Dose = Ref Date – (First Dose Date) + 1

Study Treatment Start and Stop Dates
• In this study, participants who permanently discontinue blinded study treatment may continue in the study attending the remaining visits and completing the scheduled assessments. • Data displays will state if on-treatment, post-treatment, or both on-treatment and post-treatment data are included in the summary or analysis, when applicable. • Treatment Start Date will be defined as the earliest treatment start date and Treatment Stop Date will be defined as the latest treatment stop date (from the study treatment compliance eCRF log and treatment discontinuation eCRF page). These dates will be used to determine whether a measurement is on-treatment or post-treatment. (See Section 10.4.1 Study Phases).

10.6.2. Study Population

Demographics
Age
• Age will be calculated in the IVRS and imported from the IVRS into the clinical database. The IVRS will use GSK standard IDSL algorithms to calculate age. • Only month and year of birth will be collected in accordance with GSK policy. A complete birth date will be imputed by using the month and year recorded by the IVRS and assigning a day value of '15'. Any participant with a missing month will have day and month imputed as '30 June'. • Age, in whole years, will be calculated with respect to the date of Screening (Visit 1). • 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.
Body Mass Index (BMI)
• BMI will be calculated in the eCRF as Weight (kg) / Height $(m)^2$.
Race

• The five high level Food and Drug Administration (FDA) race categories and designated Asian subcategories are:
  1. African American/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 exists)

Demographics

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 five of the high level race categories and the two 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 per IDSL will be summarized along with categories for mixed race. The categories are:
  1. African American/African Heritage
  2. American Indian or Alaska Native
  3. Asian - Central/South Asian Heritage
  4. Asian – East Asian Heritage
  5. Asian – Japanese Heritage
  6. Asian – South East Asian Heritage
  7. Asian – Mixed Race
  8. Native Hawaiian or other Pacific Islander
  9. White – Arabic/North African Heritage
  10. White – White/Caucasian/European Heritage
  11. White – Mixed Race
  12. Mixed Race
- "Asian – Mixed Race" is only used if more than one Asian category is selected, but no non-Asian races. Similarly, "White – Mixed Race" is only used if both of the White categories are selected, and no non-White races. 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%.

Treatment Compliance

- Treatment compliance, calculated as a percentage, will be based on the total number of inhalations taken from the blinded study drug inhaler(s) and the expected number of inhalations to be taken.
- The expected number of inhalations will be derived as the expected number of inhalations per day (1 for OD dosing) multiplied by the number of days on blinded study drug based on treatment start date and treatment stop date.
- The total number of inhalations taken will be based on the dose counters of the inhalers, which are re-supplied during the study. If there is no dose counter information at all then the compliance will be missing, however, as long as the information from one dose counter is present, treatment compliance will be calculated. If a dose counter start count is missing then it will be assumed to be 30. All inhalers dispensed will be used, provided the dose counter stop counts are non-missing.
- Treatment compliance will be calculated based on the formula (multiplied by 100):

$$Compliance = \left(\frac{Total \quad Number \quad of \quad Inhalations \quad Taken}{Expected \quad Inhalations \times (Stop \quad Date - Start \quad Date + 1)} \right)$$

Treatment Compliance

where *Total Number of Inhalations Taken* is the total number of doses taken from all inhalers, *Expected Inhalations* is equal to 1 and *Start Date* and *Stop Date* are the earliest treatment start date and the latest treatment stop date recorded for all of the inhalers used in the calculation.

Extent of Exposure and Study Duration

- Duration of exposure to blinded study drug will be calculated as:
  - Duration of Exposure (days) = Treatment Stop Date – Treatment Start Date + 1
- Duration of post-treatment time spent in the study will be calculated as:
  - Duration of Post-Treatment Study Time (days) = Study Conclusion Date – Treatment Stop Date
- Duration of total time spent in the study will be calculated as:
  - Duration of Study Time (days) = Study Conclusion Date – Treatment Start Date + 1
- Treatment start and stop dates used will be the earliest (start) and latest (stop) of all dates recorded for the participant. Study conclusion is defined as completion or withdrawal, as applicable.

10.6.3. Efficacy

Spirometry

Weighted Mean FEV_1 (0-4 hours)

- Serial spirometry at Week 12 (Visit 6) will be performed pre-dose and post-dose after 30 minutes and 1, 2, 3 and 4 hours of blinded study drug administration.
- Post-treatment serial spirometry will be performed pre-dose and post-dose administration of maintenance asthma medication prescribed after study treatment discontinuation for participants discontinuing blinded study treatment and continuing in the study.
- Weighted mean FEV_1 will be calculated over the nominal 0-4 hours post-dose period. Values from post-dose assessments which are before the time of dosing or 4.5 hours after the time of dosing based on actual times will be excluded from the calculation. Both the pre-dose and final value (4-hour) as well as one of the intermediate (30 minutes, 1, 2 and 3 hour) values must be present for the weighted mean to be calculated. Otherwise the endpoint will be treated as missing.
- If one or more observations are missing between 2 non-missing observations (but within the constraints noted above), the value(s) will be linearly interpolated between the 2 non-missing values.
- Weighted means will be derived by calculating the area under the FEV_1 time curve (AUC) over the nominal timepoints using the trapezoidal rule, and then dividing by the actual time between dosing and the final assessment. For post-dose observations, the actual time of assessment relative to the time of dosing will be used for the calculation.
- AUC will be calculated as the $AUC_{(t_0-t_L\ \text{hrs})}$ as follows:

$$AUC_{(t_0-t_L\ \text{hrs})} = \frac{1}{2}\sum_{i=0}^{L-1}(C_i + C_{i+1})(t_{i+1} - t_i)$$

where,

- i = collected measurement
- L = last collected measurement
- C_i = result of collected measurement i
- t_i = actual time of assessment for collected measurement i
- Weighted mean (WM) will then be calculated as follows:

$$WM_{(t_0-t_L\ \text{hrs})} = AUC_{(t_0-t_L\ \text{hrs})} / (t_L - t_0)$$

Spirometry
Morning Pre-dose FEV_1
• Change from baseline in AM FEV_1 at Week 12 (Visit 6) will be defined using the pre-dose serial spirometry assessment at the Week 12 clinic visit. Change from baseline in AM FEV_1 at Week 4 (Visit 4) and Week 8 (Visit 5) will be defined using the single pre-dose FEV_1 assessment. • On-treatment assessments collected at the Week 12 clinic visit, as well as the Week 4 (Visit 4) and Week 8 (Visit 5) clinic visits, and post-treatment assessments collected at these visits for participants who discontinue blinded study treatment and continue in the study will be included in the summaries and repeated measures analyses.

Diary
General
• AM PEF values and PM PEF values are summarized as the mean of the non-missing daily diary recordings during the time period being assessed for each participant. • Percentages of symptom-free and percentages of rescue-free 24-hour periods are calculated as the number of 24-hour periods on which a participant recorded no symptoms or no use of albuterol/salbutamol divided by the length of the time period being assessed (with non-missing values of symptoms or rescue medication recorded, respectively) x 100. See Section 10.7.2 Handling of Missing Data for details of assignment of a 24-hour period as symptom-free or rescue-free across the daytime and night-time diary recordings.
AM PEF and Percentage of Rescue-Free 24-Hour Periods – ITT (5-11 Years Old) Population
• To evaluate the primary estimand, diary data that are from the first 84 calendar days after randomization (as defined in Appendix 3: Assessment Windows) will be included in the analysis for the Weeks 1-12 time period. All available data from Weeks 1-12 regardless of whether the participant remained on-treatment at the time of the measurement will be used. • To evaluate the secondary estimand, analyses of these endpoints will be repeated using on-treatment data. Only data that are from the first 84 calendars after randomization and are on-treatment (as defined in Appendix 3: Assessment Windows and Section 10.4.1 Study Phases) will be used.
PM PEF and Percentage of Symptom-Free 24-Hour Periods – Both ITT Populations **AM PEF and Percentage of Rescue-Free 24-Hour Periods – ITT (5-17 Years Old) Population**
• Only diary data that are from the first 84 calendar days after randomization (as defined in Appendix 3: Assessment Windows) will be included in the analyses for the Weeks 1-12 time period. • All available diary data from Weeks 1-12 regardless of whether the participant remained on-treatment at the time of the measurement will be used to evaluate the primary estimand.

ACQ-5
ACQ-5 Score
• The ACQ-5 is a five-item questionnaire with response options for each question consisting of a 0 CCI [redacted] to 6 CCI [redacted] scale. • Individual questions (concerning nocturnal awakening, waking in the morning, activity limitation, shortness of breath and wheeze) are equally weighted and the ACQ-5 score is calculated as the mean of the 5 item responses. • On-treatment assessments collected at Weeks 12 and 24 (Visits 6 and 9) and post-treatment assessments collected at these visits for participants who discontinue blinded study treatment and continue in the study will be included in the analyses to evaluate the primary estimand.

Asthma Exacerbations
General
• An exacerbation is defined as deterioration of asthma requiring the use of systemic corticosteroids (tablets, suspension or injection) for at least three days or a single depot corticosteroid injection or an in-patient hospitalization or emergency department visit due to asthma that required systemic corticosteroids. • Asthma exacerbations will not be recorded as an AE unless they meet the definition of an SAE. An asthma exacerbation does not require withdrawal of the participant from blinded study treatment (or from the study). • On-treatment and post-treatment exacerbations collected during the study period will be included in the summaries to evaluate the primary estimand.

10.6.4. Safety

Adverse Events
• Adverse events will be coded using the current MedDRA coding dictionary at the time of reporting providing a Preferred Term (PT) and a System Organ Class (SOC) for analysis and reporting.
Adverse Events of Special Interest
• Adverse events of special interest are defined as AEs which have specified areas of interest for FF and FF/VI. • The adverse events of special interest groups, their subgroups and PTs which will be counted towards each of them (groups and subgroups) will be based on the current version of MedDRA at the time of reporting and will be documented prior to unblinding the study.
Risks Plot
• Relative risks and corresponding 95% CIs will be calculated as follows (Altman, 2005): • Relative risk = (A/(A+C))/(B/(B+D)) where A = number of participants with event of interest in the FF/VI treatment group B = number of participants with event of interest in the FF treatment group C = number of participants without event of interest in the FF/VI treatment group D = number of participants without event of interest in the FF treatment group. • Standard Error(log relative risk) (SElogR) =square root of ((1/A)-(1/(A+C))+(1/B)-(1/(B+D))) • 95% CI lower limit = exponential of (log(relative risk) - (probit(0.975)*SElogR)) • 95% CI upper limit = exponential of (log(relative risk) + (probit(0.975)*SElogR)) • Relative risks and 95% CIs will not be calculated if either or both treatment groups have no events of interest.

10.7. Appendix 7: Reporting Standards for Missing Data

10.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion (as specified in the protocol) is defined as completing all visits of the study including the follow-up phone contact. • Withdrawn participants will not be replaced in the study. • All available data from participants who are withdrawn from the study will be included in listings and where possible any available data from withdrawn participants will be included in summaries or analyses, unless otherwise specified.

10.7.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: o These data will be indicated by the use of a "blank" in participant listing displays. If all data for a specific visit are missing, the visit will be excluded from the display. o Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and will be displayed as such.
MMRM Analysis	• All the available assessments taken at scheduled visits (or diary weekly/bi-weekly time periods) will be included in the repeated measures models in which missing data are not explicitly imputed but the correlation between visits for all participants is used to adjust the estimate of treatment effect taking into account any missing data.
ACQ-5	• For the ACQ-5, all questions must be answered to generate an overall score; if any individual questions are missing then the overall score will be missing.
Diary Data - General	• Efficacy endpoints relating to daily diary assessments will be calculated from all available data over the time period of interest. No imputations will be performed on missing daily diary data (excluding the missing data sensitivity analyses). • Unless otherwise stated, all diary data endpoints will be considered missing if less than 2 days (or 24-hour periods) are recorded in the time period of interest. An alternate missing data rule will be used only where specified in which endpoints are set to missing if less than 4 days (or 24-hour periods) are recorded in the time period of interest.
Diary Data – 24-Hour Period Endpoints	• Each 24-hour period incorporates a daytime assessment and a night-time assessment. • Daytime symptoms are recorded in the evening and night-time symptoms are recorded the following morning for the same 24-hour period. Therefore, daytime and night-time symptoms used to define a 24-hour period refer to a participant's recorded daytime symptoms on Study Day *n* and night-time symptoms recorded on Study Day *n+1,* with rescue medication use handled in the same manner. • In computing symptom-free 24-hour periods, a given 24-hour period will be set to "symptom-free" only if the participant's responses to both the evening and following morning assessments indicate no symptoms. Similarly, in computing rescue-free 24-hour periods, the 24-hour period will only be set to "rescue-free" if responses to both the evening and following morning assessments indicate no use of rescue medication. • If there are symptoms indicated in either the evening or following morning recordings, then that 24-hour period will be set to "not symptom-free". Similarly, if there is rescue use indicated in either the evening or following morning recordings then that 24-hour

Element	Reporting Detail
	period will be set to “not rescue-free”. • Table 2 below shows how missing data will be dealt with for symptom-free 24-hour periods and exactly the same applies to rescue-free 24-hour periods.

Table 2 Assignment of 24-Hour Periods (Symptom-Free or Not)

Assignment of 24-Hour Periods		
Symptom Scores		24-Hour Period
PM	AM	
0	≥1	Not Symptom-Free
0	0	Symptom-Free
Missing	≥1	Not Symptom-Free
0	Missing	Missing
Missing	Missing	Missing

10.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays.
Adverse Events	• The eCRF does not allow partial dates to be captured for AEs. All dates will either be complete or missing. • Completely missing start or end dates will remain missing, with no imputation applied. • Where AE onset dates are missing then the AE will be considered on-treatment.

Concomitant Medications	• The eCRF allows partial dates to be captured for concomitant medications.
	• Partial dates for any concomitant medications recorded in the eCRF will be imputed using the following convention:
	  ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month
	  ○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month.
	• The answers to the questions “Taken Prior to Study?” and “Ongoing?” which are recorded in the eCRF will also be taken into consideration to determine if the medication was started pre-treatment or continued post-treatment. In each case, should the answers suggest a different classification than the dates, the medication will be summarized in all possible classifications (pre-/during/post-treatment) in which it could conceivably have been taken.

Exacerbations	• Exacerbations are treated in the same way as AEs.

10.8. Appendix 8: Abbreviations & Trade Marks

10.8.1. Abbreviations

Abbreviation	Description
ACQ	Asthma Control Questionnaire
ACT	Asthma Control Test
ADaM	Analysis Data Model
AE	Adverse Event
AM	Ante Meridiem (Morning)
ANCOVA	Analysis of Covariance
ATC	Anatomical Therapeutical Chemical
AUC	Area Under the Curve
BMI	Body Mass Index
bpm	Beats per Minute
cACT	Childhood Asthma Control Test
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CSR	Clinical Study Report
CSV	Comma Separated Variable
DBF	Database Freeze
DBR	Database Release
DP	Decimal Places
DPI	Dry Powder Inhaler
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
ETD	Early Treatment Discontinuation
EW	Early Withdrawal
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
FEV_1	Forced Expiratory Volume in 1 Second
FF	Fluticasone Furoate
FF/VI	Fluticasone Furoate/Vilanterol
FP	Fluticasone Propionate
FU	Follow-up
GSK	GlaxoSmithKline
HARP	Harmonization for Analysis and Reporting Program
hr	Hour
ICH	International Conference on Harmonization
ICS	Inhaled Corticosteroid
IDSL	Integrated Data Standards Library
IP	Investigational Product
ITT	Intent-to-Treat
IVRS	Interactive Voice Response System
J2R	Jump to Reference
kg	Kilogram

Abbreviation	Description
KR	Kenward-Roger
L	Liter
LABA	Long-Acting Beta Agonist
L/min	Liters per Minute
LS	Least Squares
m	Meter
MAR	Missing At Random
Max	Maximum
mcg	Microgram
MCMC	Markov Chain Monte Carlo
MedDRA	Medical Dictionary for Regulatory Activities
MI	Multiple Imputation
Min	Minimum
mL	Milliliter
MMRM	Mixed Model Repeated Measures
MNAR	Missing Not At Random
OD	Once Daily
PDMP	Protocol Deviation Management Plan
PEF	Peak Expiratory Flow
PM	Post Meridiem (Evening)
PT	Preferred Term
QTc(B)	Bazett's QT Interval Corrected for Heart Rate
QTc(F)	Frederica's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RTF	Rich Text Format
SABA	Short-Acting Beta Agonist
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SD	Standard Deviation
SDTM	Study Data Tabulation Model
SOC	System Organ Class
Std Err	Standard Error
TC	Telephone Call
V	Visit
vs	Versus
US	United States
WM	Weighted Mean

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 1.69	-
Efficacy	2.1 to 2.78	2.1 to 2.20
Safety	3.1 to 3.72	3.1 – 3.2
Section	**Listings**	
ICH Listings	1 to 24	
Other Listings	25 to 32	

10.9.2. Mock Example Shell Referencing

Mock example shells for all non-unique data displays are referenced in Appendix 10: Example Mock Shells for Data Displays. Programming notes are included within the shells where necessary. All data displays (tables, figures and listings) will use the term 'Subjects' in reference to study participants.

10.9.3. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
Total Population					
Subject Disposition and Demographics					
1.1.	Total	SP1	Summary of Subject Populations	IDSL	
1.2.	Total	ES6	Summary of Reasons for Screen Failure	Journal Requirements	
1.3.	Total	IE3	Summary of Inclusion/Exclusion Criteria Deviations – All Screen Failures		
1.4.	Total	ES6	Summary of Reasons for Run-in Failure	Journal Requirements	
1.5.	Total	IE3	Summary of Inclusion/Exclusion Criteria Deviations – All Run-in Failures		
1.6.	Total	NS1	Summary of Number of Subjects by Centre Total Population	EudraCT/Clinical Operations	
1.7.	Total	DM1	Summary of Demographic Characteristics Total Population		
ITT Populations					
Subject Disposition					
1.8.	ITT (5-17 Years Old)	SD1	Summary of Study Treatment Discontinuation Intent-to-Treat (5-17 Years Old)	ICH E3	1.30
1.9.	ITT (5-17 Years Old)	ES1	Summary of End of Study Record Intent-to-Treat (5-17 Years Old)	ICH E3, FDAAA, EudraCT	1.31
1.10.	ITT (5-17 Years Old)		Summary of Attendance at Each Clinic Visit Intent-to-Treat (5-17 Years Old)		1.32
1.11.	ITT (5-17 Years Old)	NS1	Summary of Number of Subjects by Centre Intent-to-Treat (5-17 Years Old)	EudraCT/Clinical Operations	1.33

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
Protocol Deviations					
1.12.	ITT (5-17 Years Old)	IE3	Summary of Inclusion/Exclusion Criteria Deviations Intent-to-Treat (5-17 Years Old)		1.34
1.13.	ITT (5-17 Years Old)	DV1	Summary of Important Protocol Deviations Intent-to-Treat (5-17 Years Old)	ICH E3	1.35
Demographic and Baseline Characteristics					
1.14.	ITT (5-17 Years Old)	DM1	Summary of Demographic Characteristics Intent-to-Treat (5-17 Years Old)	ICH E3, FDAAA, EudraCT	1.36
1.15.	ITT (5-17 Years Old)	DM5	Summary of Race and Racial Combinations Intent-to-Treat (5-17 Years Old)	ICH E3, FDA, FDAAA, EudraCT	1.37
1.16.	ITT (5-17 Years Old)	DM6	Summary of Race and Racial Combination Details Intent-to-Treat (5-17 Years Old)		1.38
1.17.	ITT (5-17 Years Old)		Summary of Duration of Asthma and Exacerbation and Smoking History Intent-to-Treat (5-17 Years Old)		1.39
1.18.	ITT (5-17 Years Old)	MH4	Summary of Current Medical Conditions Intent-to-Treat (5-17 Years Old)	ICH E3	1.40
1.19.	ITT (5-17 Years Old)	MH4	Summary of Past Medical Conditions Intent-to-Treat (5-17 Years Old)	ICH E3	1.41
1.20.	ITT (5-17 Years Old)		Summary of Screening and Baseline Lung Function Test Results Intent-to-Treat (5-17 Years Old)		1.42
1.21.	ITT (5-17 Years Old)		Summary of Baseline Lung Function Test Results by Completion Status Intent-to-Treat (5-17 Years Old)		1.43
1.22.	ITT (5-17 Years Old)		Summary of Run-In Period ACT Scores Intent-to-Treat (5-17 Years Old)	cACT Scores for 5-11 Years Old	1.44

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
Concomitant Medications					
1.23.	ITT (5-17 Years Old)	CM8b	Summary of Asthma Concomitant Medications Taken Pre-Treatment Intent-to-Treat (5-17 Years Old)	ICH E3	1.45
1.24.	ITT (5-17 Years Old)	CM8b	Summary of Asthma Concomitant Medications Taken During Treatment Intent-to-Treat (5-17 Years Old)	ICH E3	1.46
1.25.	ITT (5-17 Years Old)	CM8b	Summary of Asthma Concomitant Medications Taken Post Treatment Intent-to-Treat (5-17 Years Old)	ICH E3	1.47
1.26.	ITT (5-17 Years Old)	CM8b	Summary of Non-Asthma Concomitant Medications Taken During Treatment Intent-to-Treat (5-17 Years Old)	ICH E3	1.48
1.27.	ITT (5-17 Years Old)	CM8b	Summary of Non-Asthma Concomitant Medications Taken Post Treatment Intent-to-Treat (5-17 Years Old)	ICH E3	1.49
Exposure and Treatment Compliance					
1.28.	ITT (5-17 Years Old)	EX1	Summary of Exposure to Study Treatment and Study Duration Intent-to-Treat (5-17 Years Old)	ICH E3	1.50
1.29.	ITT (5-17 Years Old)		Summary of Treatment Compliance Intent-to-Treat (5-17 Years Old)		1.51
Subgroups					
Demographics and Baseline Characteristics					
1.52.	ITT (5-17 Years Old)	DM1	Summary of Demographic Characteristics by Age Group		
1.53.	ITT (5-17 Years Old)	DM1	Summary of Demographic Characteristics by Gender		
1.54.	ITT (5-17 Years Old)	DM1	Summary of Demographic Characteristics by Race		

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
1.55.	ITT (5-17 Years Old)	DM1	Summary of Demographic Characteristics by Ethnicity		
1.56.	ITT (5-17 Years Old)	DM1	Summary of Demographic Characteristics by Geographical Region		
1.57.	ITT (5-17 Years Old)		Summary of Duration of Asthma and Exacerbation and Smoking History by Age Group		
1.58.	ITT (5-17 Years Old)		Summary of Duration of Asthma and Exacerbation and Smoking History by Gender		
1.59.	ITT (5-17 Years Old)		Summary of Duration of Asthma and Exacerbation and Smoking History by Race		
1.60.	ITT (5-17 Years Old)		Summary of Duration of Asthma and Exacerbation and Smoking History by Ethnicity		
1.61.	ITT (5-17 Years Old)		Summary of Duration of Asthma and Exacerbation and Smoking History by Geographical Region		
1.62.	ITT (5-17 Years Old)		Summary of Screening and Baseline Lung Function Test Results by Age Group		
1.63.	ITT (5-17 Years Old)		Summary of Screening and Baseline Lung Function Test Results by Gender		
1.64.	ITT (5-17 Years Old)		Summary of Screening and Baseline Lung Function Test Results by Race		
1.65.	ITT (5-17 Years Old)		Summary of Screening and Baseline Lung Function Test Results by Ethnicity		
1.66.	ITT (5-17 Years Old)		Summary of Screening and Baseline Lung Function Test Results by Geographical Region		

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
COVID-19 Pandemic Displays					
1.67.	ITT (5-17 Years Old)	SD1	Summary of Study Treatment Discontinuation by Relationship to COVID-19 Pandemic Intent-to-Treat (5-17 Years Old)		
1.68.	ITT (5-17 Years Old)	ES1	Summary of End of Study Record by Relationship to COVID-19 Pandemic Intent-to-Treat (5-17 Years Old)		
1.69.	ITT (5-17 Years Old)	DV1	Summary of Important Protocol Deviations by Relationship to COVID-19 Pandemic Intent-to-Treat (5-17 Years Old)		

10.9.4. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
ITT Populations					
Weighted Mean FEV_1 (0-4 hours)					
2.1.	ITT (5-17 Years Old)		Summary of Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 On- and Post-Treatment Data – Intent-to-Treat (5-17 Years Old)		2.53
2.2.	ITT (5-17 Years Old)		Statistical Analysis of Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 On- and Post-Treatment Data – Intent-to-Treat (5-17 Years Old)		2.54
2.3.	ITT (5-17 Years Old)		Statistical Analysis of Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 Jump to Reference (J2R) Multiple Imputation Method – Intent-to-Treat (5-17 Years Old)		2.55
2.4.	ITT (5-17 Years Old)		Statistical Analysis of Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 Tipping Point Multiple Imputation Method – Intent-to-Treat (5-17 Years Old)	ITT (5-17 Years Old) Population only	
2.5.	ITT (5-17 Years Old)		Summary of P-values from Tipping Point Analysis of Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 Intent-to-Treat (5-17 Years Old)	ITT (5-17 Years Old) Population only	
2.6.	ITT (5-17 Years Old)		Statistical Analysis of Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 On-Treatment Data – Intent-to-Treat (5-17 Years Old)	ITT (5-17 Years Old) Population only	
2.7.	ITT (5-17 Years Old)		Statistical Analysis of Individual Serial FEV_1 (L) at Week 12 On-Treatment Data – Intent-to-Treat (5-17 Years Old)		2.56
AM PEF					
2.8.	ITT (5-17 Years Old)		Summary of Change from Baseline in AM PEF (L/min) Over Weeks 1-12 On- and Post-Treatment Data – Intent-to-Treat (5-17 Years Old)		2.31

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
	ITT (5-11 Years Old)		Summary of Missing Data for AM PEF (L/min) Over Weeks 1-12 On- and Post-Treatment Data – Intent-to-Treat (5-11 Years Old)	ITT (5-11 Years Old) Population only	2.32
2.9.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in AM PEF (L/min) Over Weeks 1-12 On- and Post-Treatment Data – Intent-to-Treat (5-17 Years Old)		2.33
2.10.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in AM PEF (L/min) Repeated Measures Averaged Over Weeks 1-12 – Intent-to-Treat (5-17 Years Old)		2.34
2.11.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in AM PEF (L/min), Weeks 1-12 Jump to Reference (J2R) Multiple Imputation Method – Intent-to-Treat (5-17 Years Old)		2.35
	ITT (5-11 Years Old)		Statistical Analysis of Change from Baseline in AM PEF (L/min) Over Weeks 1-12 On-Treatment Data – Intent-to-Treat (5-11 Years Old)	ITT (5-11 Years Old) Population only	2.36
Percentage of Rescue-Free 24-Hour Periods					
2.12.	ITT (5-17 Years Old)		Summary of Change from Baseline in Percentage of Rescue-Free 24-Hour Periods Over Weeks 1-12 On- and Post-Treatment Data – Intent-to-Treat (5-17 Years Old)		2.37
	ITT (5-11 Years Old)		Summary of Missing Data for Percentage of Rescue-Free 24-Hour Periods Over Weeks 1-12 On- and Post-Treatment Data – Intent-to-Treat (5-11 Years Old)	ITT (5-11 Years Old) Population only	2.38
2.13.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in Percentage of Rescue-Free 24-Hour Periods Over Weeks 1-12 On- and Post-Treatment Data – Intent-to-Treat (5-17 Years Old)		2.39
2.14.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in Percentage of Rescue-Free 24-Hour Periods Repeated Measures Averaged Over Weeks 1-12 – Intent-to-Treat (5-17 Years Old)		2.40

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
2.15.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in Percentage of Rescue-Free 24-Hour Periods, Weeks 1-12 Jump to Reference (J2R) Multiple Imputation Method – Intent-to-Treat (5-17 Years Old)		2.41
	ITT (5-11 Years Old)		Statistical Analysis of Change from Baseline in Percentage of Rescue-Free 24-Hour Periods Over Weeks 1-12 On-Treatment Data – Intent-to-Treat (5-11 Years Old)	ITT (5-11 Years Old) Population only	2.42
Percentage of Symptom-Free 24-Hour Periods					
2.16.	ITT (5-17 Years Old)		Summary of Change from Baseline in Percentage of Symptom-Free 24-Hour Periods Over Weeks 1-12 – On- and Post-Treatment Data Intent-to-Treat (5-17 Years Old)		2.43
2.17.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in Percentage of Symptom-Free 24-Hour Periods Over Weeks 1-12 – On- and Post-Treatment Data Intent-to-Treat (5-17 Years Old)		2.44
2.18.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in Percentage of Symptom-Free 24-Hour Periods Over Weeks 1-12 Repeated Measures Averaged Over Weeks 1-12 – Intent-to-Treat (5-17 Years Old)		2.45
2.19.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in Percentage of Symptom-Free 24-Hour Periods, Weeks 1-12 Jump to Reference (J2R) Multiple Imputation Method - Intent-to-Treat (5-17 Years Old)		2.46
Morning FEV_1					
2.20.	ITT (5-17 Years Old)		Summary of Change from Baseline in Morning FEV_1 (L) On- and Post-Treatment Data - Intent-to-Treat (5-17 Years Old)		2.47
2.21.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in Morning FEV_1 (L) On- and Post-Treatment Data - Intent-to-Treat (5-17 Years Old)		2.48
2.22.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in Morning FEV_1 (L) at Week 12 Jump to Reference (J2R) Multiple Imputation Method - Intent-to-Treat (5-17 Years Old)		2.49

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
ACQ-5					
2.23.	ITT (5-17 Years Old)		Summary of Change from Baseline in ACQ-5 Score On- and Post-Treatment Data - Intent-to-Treat (5-17 Years Old)		2.50
2.24.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in ACQ-5 Score On- and Post-Treatment Data - Intent-to-Treat (5-17 Years Old)		2.51
2.25.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in ACQ-5 Score at Week 24 Jump to Reference (J2R) Multiple Imputation Method - Intent-to-Treat (5-17 Years Old)		2.52
Exacerbations					
2.26.	ITT (5-17 Years Old)		Summary of Asthma Exacerbations Over Weeks 1-24 On- and Post-Treatment Data - Intent-to-Treat (5-17 Years Old)		2.57
Evening PEF					
2.27.	ITT (5-17 Years Old)		Summary of Change from Baseline in PM PEF (L/min) Over Weeks 1-12 On- and Post-Treatment Data - Intent-to-Treat (5-17 Years Old)		2.58
2.28.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in PM PEF (L/min) Over Weeks 1-12 On- and Post-Treatment Data -Intent-to-Treat (5-17 Years Old)		2.59
2.29.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in PM PEF (L/min) Repeated Measures Averaged Over Weeks 1-12 – Intent-to-Treat (5-17 Years Old)		2.60
2.30.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in PM PEF (L/min), Weeks 1-12 Jump to Reference (J2R) Multiple Imputation Method – Intent-to-Treat (5-17 Years Old)		2.61
Subgroups					
Weighted Mean FEV1 (0-4 hours)					
2.62.	ITT (5-17 Years Old)		Summary of Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 by Age Group		

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
2.63.	ITT (5-17 Years Old)		Summary of Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 by Gender		
2.64.	ITT (5-17 Years Old)		Summary of Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 by Race		
2.65.	ITT (5-17 Years Old)		Summary of Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 by Ethnicity		
2.66. A	ITT (5-17 Years Old)		Summary of Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 by Geographical Region		
AM PEF					
2.67.	ITT (5-17 Years Old)		Summary of Change from Baseline in AM PEF (L/min) Over Weeks 1-12 by Age Group		
2.68.	ITT (5-17 Years Old)		Summary of Change from Baseline in AM PEF (L/min) Over Weeks 1-12 by Gender		
2.69.	ITT (5-17 Years Old)		Summary of Change from Baseline in AM PEF (L/min) Over Weeks 1-12 by Race		
2.70.	ITT (5-17 Years Old)		Summary of Change from Baseline in AM PEF (L/min) Over Weeks 1-12 by Ethnicity		
2.71.	ITT (5-17 Years Old)		Summary of Change from Baseline in AM PEF (L/min) Over Weeks 1-12 by Geographical Region		
Percentage of Rescue-Free 24-Hour Periods					
2.72.	ITT (5-17 Years Old)		Summary of Change from Baseline in Percentage of Rescue-Free 24-Hour Periods Over Weeks 1-12 by Age Group		
2.73.	ITT (5-17 Years Old)		Summary of Change from Baseline in Percentage of Rescue-Free 24-Hour Periods Over Weeks 1-12 by Gender		

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
2.74.	ITT (5-17 Years Old)		Summary of Change from Baseline in Percentage of Rescue-Free 24-Hour Periods Over Weeks 1-12 by Race		
2.75.	ITT (5-17 Years Old)		Summary of Change from Baseline in Percentage of Rescue-Free 24-Hour Periods Over Weeks 1-12 by Ethnicity		
2.76.	ITT (5-17 Years Old)		Summary of Change from Baseline in Percentage of Rescue-Free 24-Hour Periods Over Weeks 1-12 by Geographical Region		
Additional AM PEF Tables Added in Amendment 1					
2.77.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in AM PEF (L/min) at Week 12, Repeated Measures On- and Post-Treatment Data - Intent-to-Treat (5-17 Years Old)		
2.78.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in AM PEF (L/min) at Week 12, Repeated Measures (Alternate Missing Data Rule) On- and Post-Treatment Data - Intent-to-Treat (5-17 Years Old)		

10.9.5. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
2.1.	ITT (5-17 Years Old)		Adjusted Treatment Differences for Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 Intent-to-Treat (5-17 Years Old)	ITT (5-17 Years Old) population only	
2.2.	ITT (5-17 Years Old)		Summary of P-values from Tipping Point Analysis for Weighted Mean FEV_1 (0-4 hours) (L) at Week 12 Intent-to-Treat (5-17 Years Old)	ITT (5-17 Years Old) Population only	

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
2.3.	ITT (5-17 Years Old)		Adjusted Mean Change from Baseline of Individual Serial FEV_1 (L) Assessments at Week 12 – On-Treatment Data Intent-to-Treat (5-17 Years Old)		2.18
2.4.	ITT (5-17 Years Old)		Mean Change from Baseline in AM PEF (L/min) – On- and Post-Treatment Data Intent-to-Treat (5-17 Years Old)		2.11
	ITT (5-11 Years Old)		Adjusted Treatment Differences for Change from Baseline in AM PEF (L/min) Over Weeks 1-12 Intent-to-Treat (5-11 Years Old)	ITT (5-11 Years Old) Population only	2.12
2.5.	ITT (5-17 Years Old)		Mean Change from Baseline in Percentage of Rescue-Free 24-Hour Periods Over Time – On- and Post-Treatment Data Intent-to-Treat (5-17 Years Old)		2.13
	ITT (5-11 Years Old)		Adjusted Treatment Differences for Change from Baseline in Percentage of Rescue-Free 24-Hour Periods Over Weeks 1-12 Intent-to-Treat (5-11 Years Old)	ITT (5-11 Years Old) Population only	2.14
2.6.	ITT (5-17 Years Old)		Mean Change from Baseline in Percentage of Symptom-Free 24-Hour Periods Over Time – On- and Post-Treatment Data Intent-to-Treat (5-17 Years Old)		2.15
2.7.	ITT (5-17 Years Old)		Repeated Measures Analysis of Change from Baseline in Morning FEV_1 (L) – On- and Post-Treatment Data Intent-to-Treat (5-17 Years Old)		2.16
2.8.	ITT (5-17 Years Old)		Repeated Measures Analysis of Change from Baseline in ACQ-5 Score – On- and Post-Treatment Data Intent-to-Treat (5-17 Years Old)		2.17
2.9.	ITT (5-17 Years Old)		Mean Change from Baseline in PM PEF (L/min) – On- and Post-Treatment Data Intent-to-Treat (5-17 Years Old)		2.19
2.10.	ITT (5-17 Years Old)		Adjusted Treatment Differences for Primary, Secondary and Other Efficacy Endpoints – On- and Post-Treatment Data Intent-to-Treat (5-17 Years Old)		2.20

10.9.6. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
ITT Populations					
Adverse Events					
3.1.	ITT (5-17 Years Old)	AE13	Adverse Event Overview Intent-to-Treat (5-17 Years Old)		3.34
3.2.	ITT (5-17 Years Old)	AE1	Summary of On-Treatment Adverse Events Intent-to-Treat (5-17 Years Old)	ICH E3	3.35
3.3.	ITT (5-17 Years Old)	AE1	Summary of Post-Treatment Adverse Events Intent-to-Treat (5-17 Years Old)	ICH E3	3.36
3.4.	ITT (5-17 Years Old)	AE3	Summary of Most Frequent On-Treatment Adverse Events Intent-to-Treat (5-17 Years Old)	ICH E3	3.37
3.5.	ITT (5-17 Years Old)	AE3	Summary of Most Frequent On-Treatment Adverse Events - Top Ten Most Commonly Reported On-Treatment Adverse Events Per Treatment Group Intent-to-Treat (5-17 Years Old)	ICH E3	3.38
3.6.	ITT (5-17 Years Old)	AE1	Summary of All Drug-Related Adverse Events Intent-to-Treat (5-17 Years Old)	ICH E3	3.39
3.7.	ITT (5-17 Years Old)	AE1	Summary of All Drug-Related Serious Adverse Events Intent-to-Treat (5-17 Years Old)	ICH E3	3.40
3.8.	ITT (5-17 Years Old)	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study Intent-to-Treat (5-17 Years Old)	IDSL	3.41
3.9.	ITT (5-17 Years Old)	AE1	Summary of On-Treatment Serious Adverse Events Intent-to-Treat (5-17 Years Old)		3.42

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
3.10.	ITT (5-17 Years Old)	AE1	Summary of Post-Treatment Serious Adverse Events Intent-to-Treat (5-17 Years Old)		3.43
3.11.	ITT (5-17 Years Old)	AE15	Summary of Common On-Treatment Non-Serious Adverse Events (>=3% without rounding) - Number of Subjects and Occurrences Intent-to-Treat (5-17 Years Old)	FDAAA, EudraCT	3.44
3.12.	ITT (5-17 Years Old)	AE16	Summary of Serious Adverse Events - Number of Subjects and Occurrences Intent-to-Treat (5-17 Years Old)	FDAAA, EudraCT	3.45
3.13.	ITT (5-17 Years Old)		Summary of On- and Post-Treatment Adverse Events of Special Interest Intent-to-Treat (5-17 Years Old)		3.46
3.14.	ITT (5-17 Years Old)		Summary of On- and Post-Treatment Serious Adverse Events of Special Interest Intent-to-Treat (5-17 Years Old)		3.47
3.15.	ITT (5-17 Years Old)		Summary of On-Treatment Pneumonia Intent-to-Treat (5-17 Years Old)		3.48
3.16.	ITT (5-17 Years Old)		Summary of Post-Treatment Pneumonia Intent-to-Treat (5-17 Years Old)		3.49
3.17.	ITT (5-17 Years Old)		Relationship of Adverse Event System Organ Class, Preferred Term and Verbatim Text Intent-to-Treat (5-17 Years Old)		3.50
3.18.	ITT (5-17 Years Old)		Record of All Preferred Terms That Could Have Mapped to Special Interest Terms Intent-to-Treat (5-17 Years Old)		3.51
Fasting Glucose					
3.19.	ITT (5-17 Years Old)		Summary of Fasting Glucose (mmol/L) Intent-to-Treat (5-17 Years Old)	ICH E3	3.52
3.20.	ITT (5-17 Years Old)		Summary of Change from Baseline in Fasting Glucose (mmol/L) Intent-to-Treat (5-17 Years Old)	ICH E3	3.53

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
3.21.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in Fasting Glucose (mmol/L) Intent-to-Treat (5-17 Years Old)		3.54
ECG					
3.22.	ITT (5-17 Years Old)	EG2	Summary of ECG Values Intent-to-Treat (5-17 Years Old)		3.55
3.23.	ITT (5-17 Years Old)	EG2	Summary of Change from Baseline in ECG Values Intent-to-Treat (5-17 Years Old)	IDSL	3.56
3.24.	ITT (5-17 Years Old)	EG1	Summary of ECG Results Interpretations Intent-to-Treat (5-17 Years Old)		3.57
3.25.	ITT (5-17 Years Old)		Summary of ECG Findings of Potential Clinical Importance Intent-to-Treat (5-17 Years Old)		3.58
3.26.	ITT (5-17 Years Old)	EG10	Summary of QTc(F) (msec) by Category Intent-to-Treat (5-17 Years Old)		3.59
3.27.	ITT (5-17 Years Old)	EG11	Summary of Change from Baseline in QTc(F) (msec) by Category Intent-to-Treat (5-17 Years Old)		3.60
3.28.	ITT (5-17 Years Old)	EG10	Summary of QTc(B) (msec) by Category Intent-to-Treat (5-17 Years Old)		3.61
3.29.	ITT (5-17 Years Old)	EG11	Summary of Change from Baseline in QTc(B) (msec) by Category Intent-to-Treat (5-17 Years Old)		3.62
3.30.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in QTc(F) (msec) Intent-to-Treat (5-17 Years Old)		3.63
3.31.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in QTc(B) (msec) Intent-to-Treat (5-17 Years Old)		3.64

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
3.32.	ITT (5-17 Years Old)		Statistical Analysis of Change from Baseline in ECG Heart Rate (bpm) Intent-to-Treat (5-17 Years Old)		3.65
Vital Signs					
3.33.	ITT (5-17 Years Old)	VS1	Summary of Vital Signs at Screening Intent-to-Treat (5-17 Years Old)	ICH E3	3.66
Subgroups					
Adverse Events					
3.67.	ITT (5-17 Years Old)	AE1	Summary of On-Treatment Adverse Events by Age Group		
3.68.	ITT (5-17 Years Old)	AE1	Summary of On-Treatment Adverse Events by Gender		
3.69.	ITT (5-17 Years Old)	AE1	Summary of On-Treatment Adverse Events by Race		
3.70.	ITT (5-17 Years Old)	AE1	Summary of On-Treatment Adverse Events by Ethnicity		
3.71.	ITT (5-17 Years Old)	AE1	Summary of On-Treatment Adverse Events by Geographical Region		
COVID-19 Pandemic Displays					
3.72.	ITT (5-17 Years Old)	PAN10	Summary of On-treatment Adverse Events Over the Time Course of the Trial (Pre, During and Post pandemic)		

10.9.1. Safety Figures

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
3.1. 1	ITT (5-17 Years Old)		Summary of Risks for FF/VI vs. FF Intent-to-Treat (5-17 Years Old)		3.2

10.9.2. ICH Listings

Note: All ICH listings will be based on the ITT (5-17 Years Old) Population.

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
Subject Disposition					
1.	ITT (5-17 Years Old)	SD2	Listing of Reasons for Study Treatment Discontinuation	ICH E3	
2.	ITT (5-17 Years Old)	ES2	Listing of Reasons for Study Withdrawal	ICH E3	
3.	ITT (5-17 Years Old)	BL1	Listing of Subjects for Whom the Treatment Blind was Broken	ICH E3	
4.	ITT (5-17 Years Old)	TA1	Listing of Randomized and Actual Treatments	ICH E3	
Protocol Deviations					
5.	ITT (5-17 Years Old)	DV2	Listing of Important Protocol Deviations	ICH E3	
6.	ITT (5-17 Years Old)	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	
Demographic and Baseline Characteristics					
7.	ITT (5-17 Years Old)	DM2	Listing of Demographic Characteristics	ICH E3	
8.	ITT (5-17 Years Old)	DM9	Listing of Race	ICH E3	

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
Concomitant Medications					
9.	ITT (5-17 Years Old)	CM3	Listing of Concomitant Medications	ICH E3	
Exposure and Treatment Compliance					
10.	ITT (5-17 Years Old)	EX3	Listing of Exposure and Compliance Data	ICH E3	
Primary Efficacy					
11.	ITT (5-17 Years Old)		Listing of FEV_1 and Weighted Mean FEV_1 (L)	ICH E3	
12.	ITT (5-17 Years Old)		Listing of Mean AM and PM PEF (L/min)	ICH E3	
Adverse Events and Pneumonia					
13.	ITT (5-17 Years Old)	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	
14.	ITT (5-17 Years Old)	AE8	Listing of On-Treatment Adverse Events	ICH E3	
15.	ITT (5-17 Years Old)	AE8	Listing of Post-Treatment Adverse Events	ICH E3	
16.	ITT (5-17 Years Old)	AE8	Listing of Adverse Events Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study	ICH E3	
17.	ITT (5-17 Years Old)	AE8	Listing of Non-Fatal Serious Adverse Events	ICH E3	
18.	ITT (5-17 Years Old)	AE8	Listing of Fatal Adverse Events	ICH E3	

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
19.	Not in ITT (5-17 Years Old)	AE8	Listing of Adverse Events for Subjects Not in the Intent-to-Treat (5-17 Years Old) Population	ICH E3	
20.	ITT (5-17 Years Old)	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	
21.	ITT (5-17 Years Old)		Listing of Pneumonia Data	ICH E3	
ECG					
22.	ITT (5-17 Years Old)	EG5	Listing of All ECG Findings for Subjects with an Abnormal ECG Finding	IDSL	
23.	ITT (5-17 Years Old)	EG3	Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance	IDSL	
24.	ITT (5-17 Years Old)	EG3	Listing of ECG Values of Potential Clinical Importance	IDSL	

10.9.3. Non-ICH Listings

Note: All Non-ICH listings will be based on the ITT (5-17 Years Old) Population.

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**ITT (5-11 Years Old) Population Display Number**
Study Population					
25.	ITT (5-17 Years Old)		Listing of Subjects who Received Incorrect Medication		
26.	ITT (5-17 Years Old)		Listing of Duration of Asthma and Exacerbation History		
27.	ITT (5-17 Years Old)		Listing of Medical Conditions		
28.	ITT (5-17 Years Old)	CM6	Listing of Relationship Between ATC Level 1, Ingredient and Verbatim Text		
Efficacy					
29.	ITT (5-17 Years Old)		Listing of Asthma Exacerbations		
Safety					
30.	ITT (5-17 Years Old)		Listing of IP Inhaler Malfunctions		
COVID-19 Pandemic Displays					
31.	ITT (5-17 Years Old)	DV2	Listing of All Non-Important COVID-19 Related Protocol Deviations		
32.	ITT (5-17 Years Old)	PAN12	Listing of COVID-19 Assessments and Symptom Assessments for Subjects with COVID-19 Adverse Events		

10.10. Appendix 10: Example Mock Shells for Data Displays

The data display shells are contained in separate documents and are available upon request.