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

Title	:	Reporting and Analysis Plan for a Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Investigate the Efficacy and Safety of Mepolizumab Administered Subcutaneously in Subjects with Moderate to Severe Atopic Dermatitis
Compound Number	:	SB240563
Effective Date	:	28-FEB-2018

Description:

- The purpose of this RAP is to describe the planned analyses and outputs to be included in the Clinical Study Report for Protocol GSK Document Number 2015N268158_02
- This RAP is intended to describe the efficacy, safety and tolerability, pharmacokinetic and pharmacodynamic analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.

RAP Author(s):

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1. INTRODUCTION

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

Revision Chronology:		
2015N268158_00	2016-AUG-25	Original
2015N268158_01	2016-DEC-26	Amendment No. 1
• Protocol amendment 1 includes recommendations from the US Food and Drug Administration (FDA) and other clarifications.		
2015N268158_02	2017-JUN-22	Amendment No. 2
• The addition of administrative interim analyses to enable review of subject efficacy and safety data summaries. • Minor clarifications regarding: collection of ECGs in triplicate for all ECG timepoints; general order of study procedures; checks for BSA and EASI eligibility utilizing eCRF auto calculated totals at Screening and Baseline visits. • Increase in anticipated number of subjects screened from approximately 75 subjects to approximately 140 subjects (no change in target number of subjects randomized). • Reminders inserted into the study schematic and Time and Events tables, indicating no IP dose will be administered at Week 16 and Week 20. • Removed requirement for subject data entry into the Daily Sign and Symptom • Severity Diary for at least 7 consecutive days immediately prior to the Baseline visit.		

Following a formal interim analysis (10-NOV-2017) after approximately 50% of subjects were randomised and had the opportunity to complete the Week 8 visit, the study met the planned futility stopping criteria and the study was terminated. As a result of the study being terminated, only a sub-set of planned protocol defined objectives and endpoints will be included for the final reporting.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

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

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
• Exploratory Objectives: Proportion of subjects who have an IGA score of 0 or 1 and at least a 2-grade improvement at each study visit by baseline blood eosinophil count • Exploratory Objectives: Mean percentage change in EASI score compared to change in blood eosinophils at each visit	• These endpoints are not being considered for final reporting	• Due to the limited responders, these endpoints will not be summarised
• Exploratory Objectives: Mean change in weekly average of daily itch/pruritus numeric rating scale [NRS] score (based on Item #1 of Daily Sign and Symptom Severity Diary) from baseline to Week 16	• This endpoint is not considered for final reporting	• Mean change from baseline for all study visit will also include Week 16 and hence this is considered as out of scope for final reporting
• Exploratory Objectives	• Additional Exploratory Objective included: Clinician Global Impression of Change is an exploratory endpoint which is not included while defining the objective/ endpoint	• This is collected as per protocol so included for final reporting
• Section 9.3.1: In all population definitions “all subjects” term is used	• In all population definition “all subjects” term has been changed to “all participants”	• Changed as per current RAP template definition
• Section 9.3.1: Per-Protocol Population definition	• Per-Protocol Population is removed	• There is no planned sensitivity analysis for the primary objective
• Section 9.3.1: PK Population definition	• PK Population definition updated	• Changed as per current RAP template definition and to take account of potential miss-dosed participants
• Section 9.1: Mentions 90% Credible Interval for the response rate and the difference in response rate for primary efficacy endpoint and later in Section 9.4 mentions as 80% Credible Interval for the response rate and the difference in response rate	• 80% Credible Interval for the response rate and the difference in response rate is provided for primary efficacy endpoint	• There was inconsistency in the protocol and should be specified as 80% Credible Interval for the response rate and the difference in response rate

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

2.2.1. Protocol Defined Objectives and Endpoints

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To determine the efficacy of mepolizumab SC in subjects with moderate to severe AD	• Proportion of subjects who achieve treatment success defined as an Investigator's Global Assessment (IGA) score of 0 or 1 and at least a 2-grade improvement at Week 16.
Secondary Objectives	**Secondary Endpoints**
• To estimate the efficacy of mepolizumab SC	• Mean percentage change in Eczema Area and Severity Index (EASI) score from baseline to each study visit. • Proportion of subjects with an IGA score of 0 or 1 and at least a 2-grade improvement at each study visit.
• To describe the safety and tolerability of mepolizumab SC	• Incidence, frequency, and nature of adverse events (AEs) including local injection site reactions and systemic reactions. • Change from baseline in laboratory parameters (hematology and chemistry) and frequency of clinically significant abnormal test results. • Change from baseline in vital signs and frequency of clinically significant abnormal results. • Immunogenicity as measured by anti-mepolizumab antibodies.
Exploratory Objectives	**Exploratory Endpoints**
• To further estimate the efficacy of mepolizumab SC	• Proportion of subjects with ≥50% improvement in EASI from baseline to each study visit. • Proportion of subjects with ≥75% improvement in EASI from baseline to each study visit. • Mean change in percent of total body surface area (% BSA) affected from baseline to each study visit. • Mean change in weekly average of daily itch/pruritus numeric rating scale [NRS] score (based on Item #1 of Daily Sign and Symptom Severity Diary) from baseline to Week 16. • Mean change in weekly average of daily itch/pruritus NRS score (based on Item #1 of Daily Sign and Symptom Severity Diary) from baseline to each study visit.
• To evaluate disease flare/relapse during and after treatment with mepolizumab SC	• Proportion of subjects who have an IGA score of 3 or 4 after achieving an IGA score of 0 or 1 and at least a 2-grade improvement during the Treatment and Follow-up Periods. • Proportion of subjects who have an increase in EASI score of >=25% from baseline during the Treatment and Follow-up Periods.

Objectives	Endpoints
• To characterize the relationship between efficacy and blood eosinophil count	• Proportion of subjects who have an IGA score of 0 or 1 and at least a 2-grade improvement at each study visit by baseline blood eosinophil count. • Mean percentage change in EASI score from baseline to each study visit by baseline blood eosinophil count. • Mean percentage change in EASI score compared to change in blood eosinophils at each visit.
• To investigate the pharmacokinetics of mepolizumab in subjects with moderate to severe AD	• Plasma concentration of mepolizumab
• To investigate the pharmacodynamics of mepolizumab in the blood and in AD lesional skin biopsies	• Ratio to baseline in blood eosinophil counts • IL-5 levels (serum free and total) • Levels of circulating biomarkers in the blood including immunoglobulin (IgE), eosinophilic cationic protein (ECP), and levels of chemokines such as thymus and activation-regulated chemokine (TARC) • Gene expression biomarkers in skin biopsies
• To describe the effect of mepolizumab SC on Patient reported Outcomes (PROs)	• Change over time in Daily Sign and Symptom Severity Diary • Change over time in Patient Global Impression of Severity and Patient Global Impression of Change

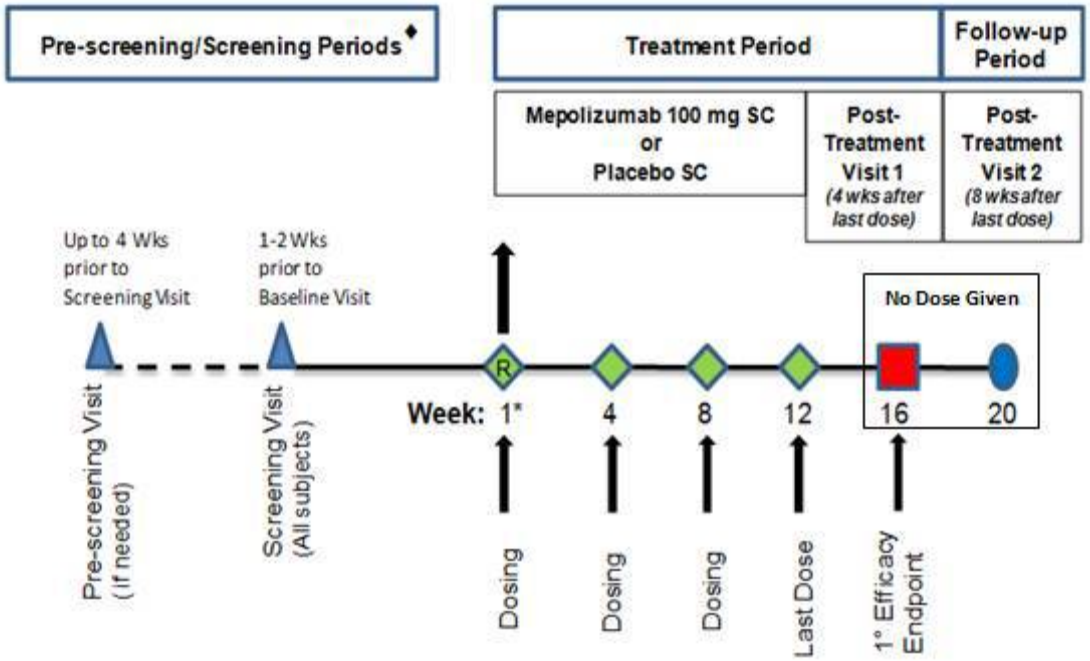
2.2.2. Final Reporting Objectives & Endpoints Following Study Termination

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To determine the efficacy of mepolizumab SC in subjects with moderate to severe AD	• Proportion of subjects who achieve treatment success defined as an Investigator's Global • Assessment (IGA) score of 0 or 1 and at least a 2-grade improvement at Week 16.
Secondary Objectives	**Secondary Endpoints**
• To estimate the efficacy of mepolizumab SC	• Mean percentage change in Eczema Area and Severity Index (EASI) score from baseline to each study visit. • Proportion of subjects with an IGA score of 0 or 1 and at least a 2-grade improvement at each study visit.
• To describe the safety and tolerability of mepolizumab SC	• Incidence, frequency, and nature of adverse events (AEs) including local injection site reactions and systemic reactions. • Change from baseline in laboratory parameters (hematology and chemistry) and frequency of clinically significant abnormal test results. • Change from baseline in vital signs and frequency of clinically significant abnormal results. • Immunogenicity as measured by anti-mepolizumab antibodies.

Objectives	Endpoints
Exploratory Objectives	**Exploratory Endpoints**
• To further estimate the efficacy of mepolizumab SC	• Proportion of subjects with ≥50% improvement in EASI from baseline to each study visit. • Proportion of subjects with ≥75% improvement in EASI from baseline to each study visit. • Mean change in percent of total body surface area (% BSA) affected from baseline to each study visit. • Mean change in weekly average of daily itch/pruritus NRS score (based on Item #1 of Daily Sign and Symptom Severity Diary) from baseline to each study visit.
• To evaluate disease flare/relapse during and after treatment with mepolizumab SC	• Proportion of subjects who have an IGA score of 3 or 4 after achieving an IGA score of 0 or 1 and at least a 2-grade improvement during the Treatment and Follow-up Periods. • Proportion of subjects who have an increase in EASI score of >=25% from baseline during the Treatment and Follow-up Periods
• To characterize the relationship between efficacy and blood eosinophil count	• Mean percentage change in EASI score from baseline to each study visit by baseline blood eosinophil count
• To investigate the pharmacokinetics of mepolizumab in subjects with moderate to severe AD	• Plasma concentration of mepolizumab
• To investigate the pharmacodynamics of mepolizumab in the blood and in AD lesional skin biopsies	• Ratio to baseline in blood eosinophil counts • IL-5 levels (serum free and total) • Levels of circulating biomarkers in the blood including immunoglobulin (IgE), eosinophilic cationic protein (ECP), and levels of chemokines such as thymus and activation-regulated chemokine (TARC) • Gene expression biomarkers in skin biopsies
• To describe the effect of mepolizumab SC on Patient reported Outcomes (PROs)	• Change over time in Daily Sign and Symptom Severity Diary • Change over time in Patient Global Impression of Severity and Patient Global Impression of Change

2.3. Study Design

Overview of Study Design and Key Features



Abbreviations: 1°= primary; R= randomize; SC= subcutaneous; wks=weeks

♦ If an ineffective treatment is stopped for the purpose of study entry, informed consent should be obtained at the time the ineffective treatment is stopped. Note: For subjects who may need to stop treatment with a biologic, the total Pre-Screening and Screening period may last up to 20 weeks (See Table 1 for prohibited period before the Screening Visit)

Design Features	• Multicenter, randomized, double-blind, placebo-controlled, 2-arm, parallel group study. • This study will consist of 4 periods: o Pre-screening (up to 4 weeks) o Screening (1 to 2 weeks) o Treatment (16 weeks with the last dose of study treatment at Week 12) o Follow-up (4 weeks). • Note: For subjects who may need to stop treatment with a biologic, the total Pre-Screening and Screening period may last up to 20 weeks.

Overview of Study Design and Key Features	
Dosing	• Study Treatment will be administered by SC injection at the Baseline visit, Week 4, Week 8, and Week 12 (last dose).
Time & Events	Refer to Appendix 1: Schedule of Activities
Treatment Assignment	Subjects will be randomized in 1:1 ratio to receive either Mepolizumab 100 mg SC or Placebo SC.
Interim Analysis	An interim analysis for futility was performed after approximately 50% of subjects were randomized and had the opportunity to complete the Week 8 visit. Futility was evaluated and pre-specified stopping criteria were met and declared for termination of the study. Further detailed in Section 3.1
Final Analysis	Final analysis is planned for subjects who had enrolled into the study prior to the termination of the study.

2.4. Statistical Hypotheses / Statistical Analyses

- No formal hypothesis testing is planned.
- The primary objective of this study is to characterize the clinical activity of mepolizumab. A Bayesian approach will be employed to estimate the posterior probability that
    1) the IGA response rate for mepolizumab is 40% or greater, and
    2) that the improvement over placebo in IGA response rate is at least 15 percentage points.
- Descriptive statistics including point estimates and corresponding 90% confidence interval and 80% credible interval will be provided for efficacy endpoints.

3. PLANNED ANALYSES

3.1. Interim Analyses

An interim analysis for futility and to enable future planning was performed after approximately 50% of subjects were randomized and had the opportunity to complete the Week 8 visit. An interim analysis was not conducted to declare early success of the study.

The interim analyses included the following data:

- An assessment of the proportion of subjects who have an IGA score of 0 or 1 and a minimum 2-grade improvement from baseline at Week 8 and later time points
- Assessments of the key secondary endpoint EASI score (change from baseline and percent change from baseline in EASI score)
- Key safety data which included Laboratory and Vital Signs data.

If a subject withdrew at a scheduled visit at which these data were not scheduled to be collected, or if a subject withdrew between scheduled visits, data were slotted to the next visit where the data were scheduled to be collected according to the study flowchart.

The criteria for futility was based on the predictive probability of success at the final analysis, given the data available at the interim analysis.

- If the posterior probability of at least a 15% difference in the IGA response rates between Mepolizumab and Placebo is greater than 70% then the study is declared successful.
- If the predicted probability of success is below the pre-specified threshold of 10%, then the study may stop for futility. i.e.,

Study Success: Success=Posterior Probability (difference in Response rates ≥ 0.15)> 70%
Stop for Futility: if Probability(Success)< 10%

Steps to calculate the Probability of Success:

- No predictions were made for data at Week 16 based on Week 8 data.
- It was deemed sufficient to use Week 8 as a surrogate for decision making at the interim based on the fact that we would require Mepolizumab to be effective at this earlier timepoint and then maintained out to Week 16.
- Markov-Chain-Monte-Carlo (MCMC) method in SAS was used to derive the posterior distributions response rate between the Mepolizumab treatment group and the placebo group.
    - From this distribution, a distribution of predicted number of responses post interim was calculated for each treatment group.
    - The observed and predicted number of responders was added together to give a large number of predicted datasets which was analysed using PROC MCMC and the same Bayesian model with non-informative prior as above but with the "observed" final data being a combination of the observed data at the interim and the predicted data from the posterior distribution at the interim.
    - The posterior probability of the response rate for Mepolizumab meeting the above criteria and the posterior probability of success at the end of the study was calculated and summarised accordingly.
- Convergence diagnostics of MCMC sample was checked using the DIAGNOSTICS option in SAS.

Additional statistical summaries were calculated to enable future planning:

- The 80% credible intervals for the response rate and difference in response rate was presented.
- The predicted posterior probability of at least a 50% response rate on Mepolizumab is greater than 60% was calculated based on observed data at the interim.

Pre-specified stopping criteria for futility were met during this analysis. There were no safety concerns. Study team had therefore terminated this study.

3.2. Final Analyses

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

1. All participants who had enrolled into the study prior to the termination of the study as defined in the protocol will be part of final analysis.
2. All required database cleaning activities have been completed and final database release (DBR) has been declared by Data Management.
3. All protocol deviations have been confirmed.
4. All criteria for unblinding the randomisation codes have been met.
5. Source Data Lock has been declared by Data Management.
6. Randomisation codes have been distributed according to RandAll NG procedures.
7. Database freeze has been declared by Data Management.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Screened	• All participants who were screened for eligibility	• Study Population
Enrolled	• All participants who passed screening and entered the study including randomized participants **Note**: Screening failures (who never passed screening even if rescreened) and participants screened but never enrolled into the study (Reserve, Not Used) are excluded from the Enrolled population as they did not enter the study.	• Study Population
Intent-to-Treat	• Comprises of all participants who are randomized and who received at least one dose of study treatment. **Note:** This population will be based on the treatment the participants are randomized to.	• Study Population • Efficacy
Safety	• Comprises of all participants who received at least one dose of a study treatment will be included in the safety population. **Note:** This population will be based on the treatment the participants actually received.	• Safety
PK	• All participants in the Safety population who received the active study treatment and had at least 1 non-missing PK assessment (Non-quantifiable [NQ] values will be considered as non-missing values).	• PK
PD	• Comprises of all participants in the ITT population who received at least one dose of study treatment and who also have a baseline serum PD measurement and at least one post-treatment serum PD measurement.	• PD

Population	Definition / Criteria	Analyses Evaluated
Biopsy	• Comprises of all participants in the ITT population who have a baseline measurement and who also have at least one post-treatment PD biomarker measurement derived from skin biopsy samples.	• Biopsy sub-study

Refer to Appendix 9: List of Data Displays which details the population used for each display.
Note: If any re-screened participants are randomized and received at least one dose then that subject will be counted in both Screened and ITT Populations.

4.1. Protocol Deviations

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

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan (10 November 2016 V1 or higher).

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

A separate listing of all inclusion/exclusion criteria deviations will also be provided. This listing will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order [1]
1	Placebo SC	Placebo SC	1
2	Mepolizumab 100 mg SC	Mepolizumab 100 mg SC	2

NOTES:

1. Order represents treatments being presented in TFL

5.2. Baseline Definitions

For all endpoints, the baseline value will be the latest pre-dose assessment. In case of missing pre-dose assessment screening would be considered as baseline. If both are missing, then baseline would be set to missing.

Parameter	Study Assessments Considered as Baseline		Baseline Used in Data Display
	Screening [1]	Day 1 (Baseline)	
Efficacy Assessments			
IGA	X	X	Day 1 (Baseline)
EASI	X	X	Day 1 (Baseline)
%BSA Affected	X	X	Day 1 (Baseline)
Daily Sign and Symptom Severity Diary (only for item #1) [2]	X	X	
Patient Global Impression of Severity		X	Day 1 (Baseline)
Safety Assessments			
Vital Signs	X	X	Day 1 (Baseline)
Haematology with differential Clinical Chemistry	X	X	Day 1 (Baseline)
ECG	X		Screening
Laboratory Assessments			
Immunogenicity (blood samples)		X	Day 1 (Baseline)
[1] Screening = 1-2 Wks Prior to Baseline Visit (All Participants). [2] Baseline for Daily Sign and Symptom Severity Diary (only for item #1) is based on derivation mentioned in Section 12.2.1			

5.2.1. Derivations and Handling of Missing Baseline Data

For untransformed data, change from baseline at each time point is expressed as a difference (value at time point – value at baseline). For log transformed data, change from baseline at each time point is expressed as a ratio (value at time point/value at baseline).

Definition	Reporting Details
Change from Baseline [1]	= Post-Baseline Visit Value – Baseline Value
% Change from Baseline [1]	= 100 x [(Post-Baseline Visit Value – Baseline) / Baseline]
Ratio to Baseline [2]	= Post-Baseline Visit Value/Baseline
[1] If the baseline value is missing the change from baseline derivations will also be missing [2] Ratio to baseline = Back transformed change from baseline of the loge transformed values	

5.3. Other Considerations for Data Analyses and Data Handling Conventions

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

Section	Component
Section 12.2	Appendix 2: Assessment Windows
Section 12.3	Appendix 3: Study Phases and Treatment Emergent Adverse Events
Section 12.4	Appendix 4: Data Display Standards & Handling Conventions
Section 12.5	Appendix 5: Derived and Transformed Data
Section 12.6	Appendix 6: Reporting Standards for Missing Data
Section 12.7	Appendix 7: Values of Potential Clinical Importance

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the "Screened", "Enrolled" and "ITT" population, unless otherwise specified.

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

7. EFFICACY ANALYSES

7.1. Primary Efficacy Analyses

7.1.1. Endpoint / Variables

- Proportion of subjects who achieve treatment success defined as an IGA score of 0 or 1 and at least a 2-grade improvement at Week 16

7.1.2. Summary Measure

Posterior mean and median response rate and difference between mepolizumab and placebo and the 80% credible interval for the response rate and the difference in response rate will be presented.

7.1.3. Strategy for Intercurrent (Post-Randomization) Events

There are no planned strategies for intercurrent events.

7.1.4. Population of Interest

The primary efficacy analyses will be based on the "Intent-To-Treat" population, unless otherwise specified.

7.1.5. 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 / variables defined in Section 7.1.1 will be summarised using descriptive statistics and listed.

7.1.5.1. Statistical Methodology Specification

Endpoint
• Proportion of subjects who achieve treatment success defined as an IGA score of 0 or 1 and at least a 2-grade improvement at Week 16
Model Specification
• A non-informative prior will be assumed for the response rate for Mepolizumab and Placebo. • Markov-Chain-Monte-Carlo (MCMC) method in SAS will be used to derive the posterior distributions for the response rates for Mepolizumab and placebo treatment groups and the difference in response rates between the Mepolizumab and placebo.
Model Checking & Diagnostics
• Convergence diagnostics of MCMC sample will be checked using the DIAGNOSTICS option in SAS and the alternative method may be used in case convergence is not achieved.
Model Results Presentation
• Posterior mean and median response rate and difference between mepolizumab and placebo and the 80% credible interval for the response rate and the difference in response rate will be presented. • The posterior probability that the IGA response rate for mepolizumab is 40% or greater and that the improvement over placebo is at least 15 percentage points will be calculated.
Sensitivity and Supportive Analyses
• There are planned sensitivity or supportive analyses.

7.2. Secondary Efficacy Analyses

7.2.1. Endpoint / Variables

- EASI Score
- IGA Response rate

7.2.2. Summary Measure

- Mean Change from baseline & percentage change from baseline EASI score to each visit
- Proportion of subjects with an IGA score of 0 or 1 and at least a 2-grade improvement from baseline to each visit

7.2.3. Strategy for Intercurrent (Post-Randomization) Events

There are no planned strategies for intercurrent events.

7.2.4. Population of Interest

The secondary efficacy analyses will be based on the "Intent-To-Treat" population, unless otherwise specified.

7.2.5. 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 / variables defined in Section 7.2.1 will be summarised using descriptive statistics and listed.

7.2.5.1. Statistical Methodology Specification

There will be no planned statistical analysis.

7.3. Exploratory Efficacy Analyses

7.3.1. Endpoint / Variables

- At least 50% and 75% improvement in EASI score from baseline
- Total body surface area (% BSA)
- Weekly average of daily itch/pruritus NRS score (based on Item #1 of Daily Sign and Symptom Severity Diary)
- IGA score of 3 or 4 after achieving an IGA score of 0 or 1 and at least a 2-grade improvement during the Treatment and Follow-up Periods.
- Increase in EASI score of >=25% from baseline during the Treatment and Follow-up Periods.
- EASI score by baseline blood eosinophil count
- Daily Sign and Symptom Severity Diary
- Patient Global Impression of Change
- Patient Global Impression of Severity
- Clinician Global Impression of Change

7.3.2. Summary Measure

- Proportion of subjects with ≥50% improvement (i.e., -50% percent change from baseline) in EASI from baseline to each visit.
- Proportion of subjects with ≥75% improvement (i.e., -75% percent change from baseline) in EASI from baseline to each visit.
- Mean change in weekly average of daily itch/pruritus NRS score (based on Item #1 of Daily Sign and Symptom Severity Diary) from baseline to each visit.

- Mean Percentage Change in EASI score from Baseline to each visit by baseline blood eosinophil count quartiles.
- Only listings will be presented for [1] IGA score of 3 or 4 after achieving an IGA score of 0 or 1 and at least a 2-grade improvement during the Treatment and Follow-up Periods, [2] Increase in EASI score of >=25% from baseline during the Treatment and Follow-up Periods. [3] Total body surface area (% BSA), [4] Daily Sign and Symptom Severity Diary, [5] Patient Global Impression of Change and Severity and [6] Clinician Global Impression of Change endpoints.

7.3.3. Strategy for Intercurrent (Post-Randomization) Events

There are no planned strategies for intercurrent events.

7.3.4. Population of Interest

The exploratory efficacy analyses will be based on the "Intent-To-Treat" population, unless otherwise specified.

7.3.4.1. 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 7.3.1 will be summarised using descriptive statistics and listed.

7.3.4.2. Statistical Methodology Specification

There will be no statistical analysis, only descriptive statistics will be presented.

8. SAFETY ANALYSES

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

8.1. Adverse Events Analyses

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

8.2. Adverse Events of Special Interest Analyses

Adverse events of special interest (AESIs) are adverse events associated with the identified and potential risks of mepolizumab. AESIs reported by the investigator as anaphylaxis reactions, systemic reactions (further categorised by the investigator as either allergic (type I hypersensitivity) or other systemic reactions) and local injection site reactions are collected via targeted eCRF within the study.

The AESIs of opportunistic infections, malignancies, serious CVT events and serious ischemic events will be identified from a list of relevant preferred terms maintained within a project level reference dataset; created based on the latest version of the MedDRA dictionary available at the time of database freeze for this study.

Separate summary tables showing the number and percent of subjects with type of AESI, broken down by preferred term will be created if at least one event is reported for an AESI category. For each type of AESI a profile summary table will be produced containing information including, but not limited to, the number of occurrences of the event, event characteristics, time to onset, intensity, outcome and action taken if more than one event is reported for an AESI category.

Listings of AESIs identified by the investigator as anaphylaxis, allergic (type I hypersensitivity), other systemic reactions and local injection site reactions, opportunistic infections, malignancies, serious CVT events and serious ischemic events if more than one event is reported under each AESI category.

The 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.

8.3. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Haematology laboratory tests and liver function tests will be based on GSK Core Data Standards. A scatter plot of maximum ALT vs baseline ALT, and maximum ALT vs total bilirubin will be produced. In addition, if any liver stopping or liver monitoring events occur during the study, then only listing of liver monitoring/stopping event reporting and hepatobiliary laboratory abnormalities will be produced. The details of the planned displays are in Appendix 9: List of Data Displays.

8.4. Other Safety Analyses

The analyses of non-laboratory safety test results including ECGs and vital signs will be based on CDISC Data Standards, unless otherwise specified. The details of the planned displays are presented in Appendix 9: List of Data Displays.

8.4.1. ECG

All sites used a standardised ECG equipment provided by a centralised external vendor. A central ECG reader was used. The site and vendor provided ECG interpretation, while the site differentiates between “Abnormal – Not Clinically Significant and Abnormal – Clinically significant”, the vendor only specifies ‘Abnormal’. There are differences between the site vs vendor interpretations (i.e. the site interpretation = abnormal vs vendor = normal and site = normal vs vendor = abnormal).

As site interpretations also take into consideration assessment from investigators of patients, the site interpretations will be used for summaries (i.e. even though for patients, vendor = abnormal vs site = normal) but both the site and vendor interpretations will be listed.

Actual and change from baseline QTcF category values will be summarized for each visit. Actual QTcF value is categorized as: <=450, >450 to <=480, >480 to <=500, and >500. Change from baseline QTcF value is categorized as: <=30, >30 to ≤ 60 and >60. In addition, listing will be produced for subject meeting the criteria of actual QTcF >500 msec or change from baseline >60 msec.

8.5. Immunogenicity Analyses

Immunogenicity analyses will be based on GSK Core Data Standards, unless otherwise specified. The details of the planned displays are presented in Appendix 9: List of Data Displays in Section 12.9.6.

An immune response to a therapeutic drug can lead to generation of anti-drug antibodies within the blood. For the immunogenicity assessment, two types of antibody assays will be performed, a binding antibody assay and a neutralizing antibody assay.

For the binding antibody assay, there will be three testing steps: screening, confirmation and titration. The screening assay produces a result of positive or negative relative to a screening cut point. Positive samples continue with the confirmation assay, which also produces a result of positive or negative relative to a confirmation cut point. For samples with a positive confirmation result, a titre value will also be obtained to quantify the degree of binding in a titration assay and the sample will be characterized as positive for the binding antibodies. Subjects who test positive for the binding antibody assay, will be tested in the neutralizing antibody assay, which also reports results as positive or negative.

Subjects will be categorized as negative or positive and positive binding antibody will be further categorized as transient positive or persistent positive at each visit and for anytime post baseline visit. Summary statistics for titer results will also be included for anytime post baseline visit.

A summary of adverse events by highest post-baseline binding antibody result will be produced. A summary of treatment emergent positive confirmation binding ADA assay results in the subset of subjects who did not have a positive confirmation binding ADA assay result prior to the dosing of study treatment will also be presented.

Neutralizing antibody assay results will be summarised by visit and will also be summarised by category (positive or negative). For anytime post baseline visit, highest result will be used, i.e. according to the following hierarchy: ADA result will be Persistent Positive > Transient Positive > Negative, NAB result will be Positive > Negative and highest titer value. A listing of all immunogenicity data will also be provided.

9. PHARMACOKINETIC ANALYSES

9.1. Exploratory Pharmacokinetic Analyses

9.1.1. Endpoint / Variables

Plasma concentration of mepolizumab.

9.1.1.1. Drug Concentration Measures

Mepolizumab plasma concentrations will be summarised and listed by nominal time. Standard summary statistics will be calculated.

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

9.1.1.2. Derived Pharmacokinetic Parameters

As a result of study termination, there will be no derivation of Pharmacokinetic Parameters for this study.

9.1.2. Summary Measure

There is no treatment comparison in this study since only one active study treatment was administered. Mepolizumab plasma Concentrations will be summarised descriptively.

9.1.3. Population of Interest

The exploratory pharmacokinetic analyses will be based on the "Pharmacokinetic" population, unless otherwise specified.

9.1.4. Strategy for Intercurrent (Post-Randomization) Events

Missing concentrations and concentrations below the limit of quantification of the assay will be handled as described in Guidance Document GUI_51487.

9.1.5. Statistical Analyses / Methods

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

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

10. PHARMACODYNAMIC AND BIOMARKER ANALYSES

10.1. Exploratory Pharmacodynamic and Biomarker Analyses

10.1.1. Endpoint / Variables

Endpoint	Parameters
Biomarker(s) / Pharmacodynamic Markers	• Blood Sample: Eosinophil counts • Blood Sample: IL5 levels (serum free and total)
Novel Biomarkers – Skin Biopsy Sub-study & Serum Biomarkers	
RNA Transcriptome Research (Cancelled)	• N/A
RNA Expression Research of a Subset of RNA Species [1]	• Gene expression biomarkers in skin biopsies
Protein Levels of Biomarkers in Serum [2]	• Total IgE, eosinophil cationic protein (ECP) and chemokines Eotaxin-1, Eotaxin-3, TARC, MCP4
[1] Epistem will be providing a report to be include in the CSR. [2] MDC was dropped as an analyte due to assay issues)	

10.1.2. Summary Measure

- Geometric Means for ratio to baseline in blood eosinophil counts and for absolute blood eosinophil count at each visit.
- Only listings will be presented for biomarker endpoints.

10.1.3. Population of Interest

The pharmacodynamics and biomarker analyses will be based on the "Safety", "Pharmacodynamic" and "Biopsy" populations, unless otherwise specified.

Safety population will be used for summarizing blood eosinophil counts. Biopsy population will be used for skin biopsy. Pharmacodynamic population will be used for remaining endpoints.

10.1.4. 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/variables defined in Section 10.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

10.1.4.1. Statistical Methodology Specification

Endpoint
• Ratio to baseline blood eosinophil counts (Note: from standard haematology assessments)
Model Specification

• Mixed Models Repeated Measures (MMRM) analysis.
• The analysis will include all measurements at scheduled visits
• Terms in the model:
• **Response**: Ratio to Baseline Blood eosinophil count (log_e transformed prior to analysis) (see Appendix 5: Derived and Transformed Data, Section 12.5.6).
  • **Categorical**: Treatment group, Visit.
  • **Continuous/covariate**: Baseline blood eosinophil count.
  • **Interaction:** Treatment group*Visit.
  • **Repeated**: Visit.
• The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used. An unstructured covariance structure for the R matrix will be used by specifying 'type=UN' on the REPEATED line.

Model Checking
• Distributional assumptions underlying the model used for analysis will be examined by obtaining a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable.
Model Results Presentation
• The results of the analysis from the MMRM model will be presented for each visit as LS Geometric Mean (SE), LS Geometric Mean Ratio to Baseline (95% Confidence Interval) for each treatment group, Geometric Treatment Ratio (Mepolizumab/Placebo) and corresponding 95% Confidence Interval.
Sensitivity and Supportive Analyses
• There are no planned sensitivity or supportive analyses.

11. REFERENCES

GlaxoSmithKline Document Number 2015N268158_02, Study ID 205050, A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Investigate the Efficacy and Safety of Mepolizumab Administered Subcutaneously in Subjects with Moderate to Severe Atopic Dermatitis. Effective Date: 22-JUN-2017.

12. APPENDICES

12.1. Appendix 1: Schedule of Activities

Time and Events Table: Pre-Screening and Screening

Period:	Pre-Screening and Screening Period		
			Notes
Visits:	Pre-Screening	Screening	
	Up to 4 wks prior to Screening Visit	1 to 2 wks prior to Day 1 Baseline Visit	• Individual Pre-Screening and Screening Visits will be conducted for subjects who have used prohibited medications or non-drug therapies and need to fulfil the prohibited medications period prior to the Screening Visit (See Table 1). For these subjects, the Pre-Screening Visit will be completed up to 4 weeks prior to the Screening Visit. After requirements regarding previous use of prohibited medication and non-drug therapies are met (See Table 1), the Screening Visit will be completed. The Screening visit will be completed up to 2 weeks prior to the Baseline visit. • Assessments for Pre-screening and Screening Periods will be combined into one Screening Visit for subjects who meet prohibited medications or non-drug therapies criteria in Table 1 at entry (total time to complete the combined assessments= 1 to 2 weeks prior to Baseline). • The period between the Screening Visit and Baseline Visit may be extended beyond 2 weeks, if needed, to obtain the results of all screening laboratory assessments. • Perform procedures in the order listed in Section 7
Procedure			
Informed consent	PS		Obtain informed consent prior to study participation. See Section 4.2.1 and Table 1 notes.
Demography	PS		
Fitzpatrick Skin Type Classification	PS		
Inclusion/exclusion criteria	PS	S	
Medical history/Medical conditions	PS	S	Includes drug and alcohol usage, smoking history, cardiovascular medical history, and family history of premature cardiovascular disease.
Safety Assessments			
Vital Signs		S	See Section 7.4.4.
Concomitant medications	PS	S	The subject must apply the same non-prescription, non-medicated emollient twice daily for the 7 consecutive days immediately prior to the Baseline visit. On study visit days,.
			emollient must not be applied within the 2-hour period preceding the study visit. If emollient is applied <2 hours prior to the visit, wait ≥2 hours after application to perform study procedures. See Section 6.10.1
Serious Adverse Events (SAEs)	PS	S	Record SAEs related to study participation or to a GSK product from the time a subject consents to participate in the study up to and including any follow-up contact. AEs will be collected from the start of study treatment until the follow-up contact (Section 7.4.1.1).
ECG		S	
Laboratory Assessments	**Note: Results of all laboratory assessments must be available prior to randomization**		
HBsAG and hepatitis C antibody	PS		Not required if test otherwise performed within 3 months prior to first dose of study treatment.
Pregnancy test (urine)	PS	S	Females of reproductive potential. If urine pregnancy test is positive, collect serum hCG (central laboratory). See Section 7.4.2 and Appendix 7 for reporting requirements.
FSH and estradiol	PS		Females, if needed to confirm postmenopausal status (See Section 5.1).
Hematology with differential		S	
Clinical Chemistry		S	
Parasitic screening		S	Parasitic screening is only required in countries with high-risk or for subjects who have visited high-risk countries in the past 6 months. Sites should use local laboratories. Selection of tests will be at the investigator's judgment.
Efficacy Assessments and Patient-Reported Outcomes			
Investigator's Global Assessment		S	See Section 7.3 and SRM for rater requirements.
% BSA affected		S	Regional assessment. Total % BSA affected will be auto-calculated within the eCRF. The total %BSA score from the eCRF will be utilized to confirm inclusion criteria. See Section 7.3 and SRM for rater requirements.
EASI		S	% BSA affected will be utilized to calculate the EASI score. The EASI score will be auto-calculated within the eCRF. The EASI score from the eCRF will be utilized to confirm inclusion criteria. See Section 7.3 and SRM for rater requirements
Daily Sign and Symptom Severity Diary (electronic)		S	To be completed by the subject every evening before 12:00 AM (midnight). If subject fails screening and does not continue in the study, the subject will return the electronic device to the site. (See SRM for guidance).

Time and Events Table: Baseline through Follow-up Period

Period:	Treatment					Follow-up Period		Notes
					Post-Tx Visit 1 *4 wks after last dose*	Post-Tx Visit 2 *8 wks after last dose*	Early WD	• Perform procedures in the order listed in Section 7. • Early WD visit: same procedures apply both to subjects discontinuing treatment but continuing with Post-Tx visits and to subjects withdrawing from the study.
Day/Week:	Day 1 Baseline	Wk 4	Wk 8	Wk 12	Wk 16 (No IP dose)	Wk 20 (No IP dose)		
Window (days):		±3	±3	±3	±3	±3		
Procedure								
Inclusion/exclusion criteria	BL							
Randomization (IVRS)	BL							
Safety Assessments								
Physical examination, height, weight	BL					20	EW	Perform/obtain pre-dose on dosing days. See Section 7.4.3.
Vital signs	BL	4	8	12	16	20	EW	Obtain pre-dose on dosing days. See Section 7.4.4.
ECG		4			16		EW	Obtain pre-dose at Week 4. Unscheduled ECGs may also be performed as clinically indicated during the study.
Concomitant medications	BL	4	8	12	16	20	EW	See Section 6.10.1. Subject must apply the same non-prescription, non-medicated emollient twice daily during Treatment and Follow-up Periods. On study visit days, emollient must not be applied within the 2-hour period preceding the study visit. If emollient is applied <2 hours prior to the visit, wait ≥2 hours after application to perform study procedures.
Adverse events	BL	4	8	12	16	20	EW	Collect AEs from the start of study treatment until the follow-up contact. Record SAEs related to study participation or to a GSK product from the time a subject consents to participate in the study up to and including any follow-up contact (Section 7.4.1.1).
Laboratory Assessments	**Note: Labs are collected pre-dose on dosing days (includes blood draws, skin biopsies, and pregnancy testing)**							
Genetic sample- pre-dose	BL							Subject participation is voluntary. Additional informed consent is required.
Hematology with differential	BL	4	8	12	16	20	EW	Total WBC, absolute eosinophil count, and differential (%) will be blinded from the Baseline visit until the end of the study.
Clinical Chemistry	BL	4	8	12	16		EW	
Pregnancy test (urine)	BL	4	8	12	16	20	EW	Females of reproductive potential. If urine pregnancy test is positive, collect serum hCG (central laboratory). See Section 7.4.2 and Appendix 7 for reporting requirements.
Pharmacokinetic blood sample		4	8	12	16	20	EW	Results will be blinded during the study.
Blood sample for immunogenicity	BL	4			16	20	EW	Results will be blinded during the study.
Serum IL-5	BL	4			16	20	EW	Results will be blinded during the study.
Serum sample for biomarkers	BL	4	8	12	16			Results will be blinded during the study.
Skin biopsy sub-study- pre-identified study centers only	BL	4						Subject participation is voluntary. Additional informed consent is required. Results will be blinded during the study. Collect 1 lesional sample (from chronic lesion) and 1 non-lesional sample at each visit.
Efficacy Assessments and Patient-Reported Outcomes								
Patient Global Impression of Change		4	8	12	16		EW	Complete pre-dose prior to other assessments or evaluation by the investigator.

Efficacy Assessments and Patient-Reported Outcomes								
Patient Global Impression of Severity	BL	4	8	12	16	20	EW	Complete pre-dose prior to other assessments or evaluation by the investigator.
Daily Sign and Symptom Severity Diary (electronic)	←----------					----------→	EW	To be completed by the subject every evening before 12:00 A.M.(midnight) during the Treatment and Follow-up Periods. Site personnel will review subject compliance with the diary at each visit.
Investigator's Global Assessment	BL	4	8	12	16	20	EW	Complete pre-dose. See Section 7.3 and SRM for rater requirements.
% BSA affected	BL	4	8	12	16	20	EW	Complete pre-dose. Regional assessment. Total % BSA affected will be auto-calculated within the eCRF. See Section 7.3 and SRM for rater requirements
EASI	BL	4	8	12	16	20	EW	Complete pre-dose. % BSA affected from each visit will be utilized to calculate the EASI score at each visit. The EASI score will be auto-calculated within the eCRF. See Section 7.3 and SRM for rater requirements
Clinician Global Impression of Change		4	8	12	16		EW	Complete pre-dose. See Section 7.3. and SRM for rater requirements
Investigational Product and Other Study Treatment								
Mepolizumab or Placebo Administration	BL	4	8	12	No IP dose	No IP dose		See Section 6.1 and Section 6.1.1 for study treatment administration details. Observation of subject required for 1 hour after administration of study treatment. See Section 6.1.2. Postponement of study treatment and visit assessment is required during course of antibiotic, antiviral or antifungal treatment for acute infection. Postponed doses can be administered no further than 2 weeks after the original scheduled dose (See Section 5.4.3).

Time and Events Table: Unscheduled Visit for Flare/Relapse

Period:	Treatment and Follow-up	
		Notes
Week:	Unscheduled	• This visit is for subjects who experience AD flare/relapse between scheduled study visits. See Section 4.2.4. • In the case of flare/relapse with intolerable AD symptoms where the use of prohibited medication is required (See Table 1), the subject will be permanently withdrawn from treatment. • If the subject permanently discontinues study treatment or withdraws from the study, the procedures and visits described in Section 5.4 and Table 3 will apply. • Perform procedures in the order listed in Section 7.
Window (days):	+5	Visit window is from the time the subject notifies the site staff of potential AD flare/relapse.
Procedure		
Safety Assessments		
Physical examination, height, weight	U	To be performed only if needed, based on the investigator's judgment.
Vital signs	U	See Section 7.4.4.
Concomitant medications	U	
Adverse events	U	See Appendix 11. The disease under study (AD) or expected progression, signs, or symptoms of AD do not meet the definition of AE unless the worsening is more severe than expected for the subject's condition.
Laboratory Assessments		
Hematology with differential	U	Total WBC, absolute eosinophil count, and differential (%) will remain blinded.
Clinical Chemistry	U	Performed only if needed, based on investigator's judgment.
Efficacy Assessments and Patient-Reported Outcomes		
Daily Sign and Symptom Severity Diary (electronic)	U	To be completed the by subject in the evening.
Investigator's Global Assessment	U	
% BSA affected	U	Regional assessment. Total % BSA affected will be auto-calculated within the eCRF. See Section 7.3 and SRM for rater requirements.
EASI	U	% BSA affected from each visit will be utilized to calculate the EASI score at each visit. The EASI score will be auto-calculated within the eCRF. See Section 7.3 and SRM for rater requirements.

Abbreviations: AEs= adverse events; BSA= body surface area; EASI= Eczema Area and Severity Index; FSH= follicle stimulating hormone; HBsAG= hepatitis B surface antigen; SAEs= serious adverse events; SRM=Study Reference Manual. AD= atopic dermatitis; EASI= Eczema Area and Severity Index; WBC= white blood cell; WD=withdrawal; IL-5= interleukin-5; Tx= Treatment; Wk=Week; wks=weeks

12.2. Appendix 2: Assessment Windows

Clinic visits are scheduled to take place as specified in the protocol. Unscheduled visit will be excluded from analyses on any population. For all clinic visits, nominal visit days and times will be used for reporting; for example, if a subject recorded value on the Week 4 visit that were made on Week 3 of treatment, they will be presented as Week 4 values.

If a subject withdraws at a scheduled visit, and these data were scheduled to be collected at that visit, the data will be summarised and analysed (as appropriate) together with data from subjects who did not withdraw. If a subject withdraws at a scheduled visit at which these data were not scheduled to be collected, or if a subject withdraws between scheduled visits, data will be slotted to the next visit where the data was scheduled to be collected according to the study flowchart. The protocol visits windows of ±3 days should be applied to the assignment of withdrawal visits, so that if a subject withdraws within the appropriate number of days from the last visit where that data was scheduled to be collected, they would get that data slotted to that visit and otherwise the data will be slotted to the next scheduled visit.

The early withdrawal visit will then be re-labelled as the corresponding visit. The same approach will be followed to Post Treatment 1 and Post Treatment 2 visits.

If there is more than one assessment associated with a particular visit interval, then the latest assessment will be used for summary tables and analyses. Where two or more findings (e.g. ECG (i.e. site interpretations will be used), laboratory data) slot to the same visit interval, the most 'abnormal' results will be used, i.e. according to the following hierarchy: Abnormal-Clinically Significant > Abnormal – not clinically significant > Normal.

12.2.1. Definitions of Assessment Windows for Analyses

The daily itch/pruritus NRS score (based on Item #1 of Daily Sign and Symptom Severity Diary) is recorded daily and will be averaged for every week.

The 7-days average score will be calculated as:

$$\frac{\sum(\text{Daily itch/pruritus NRS score in 7 days})}{\text{Total numer of days Daily itch/pruritus NRS score is recorded in 7 days}^{*}}$$

- If a subject is missing more than 3 daily itch/pruritus NRS scores out of the 7 days, then the average NRS score for that week will be recorded as missing.
- 7-days average score for baseline visit will be calculated based on 7 days prior to the day of dosing (i.e., from Day -7 to Day -1).
- 7-days average score for Week 1 visit will be 7 days after the day of dosing (i.e., from Day 1 to Day 7).
- Similarly, for Week 2 (from Day 8 to Day 14) and henceforth till Week 20.

12.3. Appendix 3: Study Phases and Treatment Emergent Adverse Events

12.3.1. Study Phases

Safety assessments and events will be classified according to the time of occurrence relative to the first dose of investigational product.

The on-treatment phase for the presentation of exposure, adverse event and concomitant medications is defined as being from the day of the first administration to the day of the last administration of study treatment + another 28 days inclusive.

Treatment Phase	Definition
Pre-Treatment	Date < IP start date
On-Treatment	Event onset date is on/after IP start date & on/before IP stop date + 28 days (IP Start Date ≤ Date ≤ IP Stop Date + 28 days)
Post-Treatment	Event onset date is after the IP stop date + 28 (Date > IP stop date + 28)
IP = Investigational Product = Study Treatment	

12.3.1.1. Study Phases for Efficacy Assessments

Efficacy assessments and events will be classified according to the time of occurrence relative to the study periods defined below:

Period	Definition
Study Treatment Period	Date ≤ Week 16 date (or date of withdrawal from the study, if prior to Week 16)
Follow-up Period	Week 16 date < Date ≤ Week 20 date (or date of withdrawal from the study, if between Week 16 and 20)

12.3.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	If AE onset date is on or after treatment start date & on or before treatment stop date. (plus 28 days) (Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date + 28)

NOTES:

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

12.4. Appendix 4: Data Display Standards & Handling Conventions

12.4.1. Reporting Process

Software	
• The currently supported versions of SAS software 9.4 or higher will be used.	
Reporting Area	
HARP Server	: uk1salx00175.corpnet2.com
HARP Compound	: sb240563\mid205050\final_02
QC Spreadsheet	: sb240563\mid205050\ final_02\documents
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.1.3 & ADaM IG Version 1.0]. • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM.	
Generation of RTF Files	
• RTF files will be generated for SAC.	

12.4.2. Reporting Standards

General

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

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

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

Unscheduled Visits	
• Unscheduled visits will not be included in summary tables and/or figures. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

12.4.3. Reporting Standards for Pharmacokinetic

Pharmacokinetic Concentration Data	
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Refer to IDSL Statistical Principle 6.06.1. Note: BLQ Concentration values will be imputed as per GUI_51487 for descriptive summary statistics and summarized graphical displays only.

12.5. Appendix 5: Derived and Transformed Data

12.5.1. General

Multiple Measurements at One Analysis Time Point
• If there are two values within a time window (as per Section 12.2.1) then the latest assessment will be used. • Participants having both High and Low values for Normal Ranges at any post-baseline visit for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

• Calculated as the number of days from Randomization Date:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < Randomization Date → Study Day = Ref Date – Randomization Date
  • Ref Data ≥ Randomization Date → Study Day = (Ref Date – Randomization Date) + 1

12.5.2. Study Population

Extent of Exposure
• Number of days of exposure to study drug will be calculated based on the formula: Duration of Exposure in Days = (Treatment Stop Date – Treatment Start Date) + 29 • Participants who were randomized but did not report a treatment start date will be categorised as having zero days of exposure. • On-treatment phase will be calculated based on the formula: On-Treatment Phase = (Treatment Stop Date – Treatment Start Date) + 29

12.5.3. Efficacy

Efficacy
Investigators Global Assessment (IGA)
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.
• A Responder is defined as a subject who has an IGA score of 0 or 1 and a minimum 2-grade improvement from baseline. This is calculated for each study visit. • As per protocol, a non-responder imputation will be used for all early withdrawal subjects where

Efficacy

subject's data will be imputed as a Non-Responder for all post withdrawal visits. This imputation will be used for summary and analysis table for primary and secondary endpoints.

- The observed IGA score classifications will be used for each visit. For all early withdrawal subjects the data from Post-Treatment 1/Post-Treatment 2/Early Withdrawal visits will be slotted using the algorithm detailed in Section 12.2
- AD flare/relapse for IGA is defined as IGA score of 3 or 4 after achieving an IGA score of 0 or 1 and at least a 2- grade improvement from the baseline.

Body Surface Area

Body Region	% Involvement (0-100% each area)	% Involvement x Proportionality Multiplier	Regional % BSA Involvement
Head and neck		____ x 0.1	
Upper extremities		____ x 0.2	
Trunk		____ x 0.3	
Lower extremities		____ x 0.4	
	Total Involved % BSA (sum of the 4 area values) =		_____

EASI

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

[redacted]

- The observed EASI data will be used for each visit. For all early withdrawal subjects, data from Post-Treatment 1/Post-Treatment 2/ Early Withdrawal visits will be slotted using the algorithm detailed in Section 12.2.
- AD flare/relapse for EASI is defined as increase in EASI score of ≥25% from Baseline.

12.5.4. Safety

Adverse Events of Special Interest
• Section 8.2: Adverse Events of Special Interest Analyses provides a full list of AEs of special interest for this compound. AESIs of anaphylaxis reactions, systemic reactions, and local injection site reactions are collected via targeted eCRF. • The AESIs of opportunistic infections, malignancies, serious CVT events and serious ischemic events will be identified from a list of relevant preferred terms maintained within a project level reference dataset; created based on the latest version of the MedDRA dictionary available at the time of database freeze for this study (See Program Safety Analysis Plan for additional details).
Laboratory Parameters
• If a laboratory value which is expected to have a numeric value for summary purposes, has a non-detectable level reported in the database, where the numeric value is missing, but typically a character value starting with '<x' or '>x' (or indicated as less than x or greater than x in the comment field) is present, the number of significant digits in the observed values will be used to determine how much to add or subtract in order to impute the corresponding numeric value. o Example 1: 2 Decimal Points = '< x' becomes x – 0.01 o Example 2: 1 Decimal Point = '> x' becomes x + 0.1 o Example 3: 0 Decimal Points = '< x' becomes x – 1
Immunogenicity (Binding Antibody Assay Results)
• Positive binding antibody assay results are to be categorised as transient positive or persistent positive accordingly to the following definitions: • For all post-baseline visits, other than final study assessment o Transient positive = a single positive immunogenic response at a visit, where the previous visit was negative o Persistent positive = a positive immunogenic response at a visit, where the previous visit was also positive • For the final assessment: • Any positive response will be considered a persistent response, regardless of the status at the previous visit

12.5.5. Pharmacokinetic

There will be no derivation of Pharmacokinetic Parameters for this study.

12.5.6. Pharmacodynamic and Biomarker

Pharmacodynamic
Blood Eosinophils
• Blood eosinophil counts will be log transformed (loge) prior to analysis. • For the log transformation values of 0 GI/L will be imputed to a value of minimum for all non-missing results/2.

12.6. Appendix 6: Reporting Standards for Missing Data

12.6.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as if he/she receives all planned doses of study treatment and completes the Week 16 (Post-Treatment 1) and Week 20 (Post-Treatment 2) visits. • Withdrawn subjects were not replaced in the study. • All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified. • Withdrawal visits will be slotted as per Appendix 2: Assessment Windows

12.6.2. Handling of Missing Data

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

12.6.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: ○ Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 3: Study Phases and Treatment Emergent Adverse Events. ○ Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.

12.7. Appendix 7: Values of Potential Clinical Importance

12.7.1. Laboratory Values

Haematology				
Laboratory Parameter	**Units**	**Age Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Hematocrit	Ratio of 1	12+	0.201	0.599
Hemoglobin	G/L	12+	71	199
Platelet Count	GI/L	1+	31	1499
While Blood Cell Count (WBC)	GI/L	12+	1.1	

Clinical Chemistry				
Laboratory Parameter	**Units**	**Age Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
ALT	U/L	3-12		>143 (and Total Bilirubin >43)
	U/L	13+		>239 (and Total Bilirubin >43)
Calcium	mmol/L	3+	1.50	3.24
Glucose	mmol/L	1+	2.2	27.8
Potassium	mmol/L	3+	2.8	6.5
Sodium	mmol/L	0+	120	160

Possible Hy's Law Cases			
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**
ALT, Bilirubin			ALT ≥ 3xULN and Bilirubin ≥ 2xULN (>35% direct)
ALT, INR			ALT ≥ 3xULN and INR > 1.5

12.7.2. Vital Signs

Vital Sign Parameter	**Units**	**Clinical Concern Range**	
		Lower	**Upper**
Absolute			
Systolic Blood Pressure	mmHg	< 85	> 160
Diastolic Blood Pressure	mmHg	< 45	> 100
Heart Rate	bpm	< 40	> 110

12.8. Appendix 8: Abbreviations & Trade Marks

12.8.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AESI	Adverse Events of Special Interest
AIC	Akaike's Information Criteria
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
DBF	Database Freeze
DBR	Database Release
DOB	Date of Birth
DP	Decimal Places
EASI	Eczema Area and Severity Index
eCRF	Electronic Case Record Form
ECP	Eosinophilic Cationic Protein
EASI	Eczema Area and Severity Index
EMA	European Medicines Agency
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
GSK	GlaxoSmithKline
IA	Interim Analysis
ICH	International Conference on Harmonization
IDSL	Integrated Data Standards Library
IGA	Investigator’s Global Assessment
IGE	Immunoglobulin
ITT	Intent-To-Treat
MCMC	Markov-Chain-Monte-Carlo
MMRM	Mixed Model Repeated Measures
NRS	Numeric Rating Scale
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PRO	Patient reported Outcomes
QC	Quality Control
RAP	Reporting & Analysis Plan
SAC	Statistical Analysis Complete
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
TARC	Activation-regulated Chemokine
TA	Therapeutic Area
TFL	Tables, Figures & Listings

12.8.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS

12.9. Appendix 9: List of Data Displays

12.9.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.10	N/A
Efficacy	2.1 to 2.7	N/A
Safety	3.1 to 3.40	3.1 to 3.2
Pharmacokinetic	4.1	4.1 to 4.2
Pharmacodynamic and Biomarker	5.1 to 5.2	5.1 to 5.2
Section	**Listings**	
ICH Listings	1 to 26	
Other Listings	27 to 40	

12.9.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 10: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Pharmacodynamic and Biomarker	PD_Fn	PD_Tn	PD_Ln

NOTES:

- Non-Standard displays are indicated in the 'IDSL / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.

12.9.3. Deliverables

Delivery [Priority] [1]	Description
SAC	Final Statistical Analysis Complete

NOTES:

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

12.9.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL/ Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.1.	ITT	ES1	Subject Status and Reason for Study Withdrawal	ICH E3, FDAAA, EudraCT	SAC
1.2.	ITT	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment	ICH E3	SAC
1.3.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements Add Footnote "Note: Re-screened participants who have been randomised are included both in ENROLLED as well as FAILED category.	SAC
1.4.	Enrolled	NS1	Summary of Number of Participants Enrolled by Country and Site ID	EudraCT/Clinical Operations	SAC
Population Analysed					
1.5.	Screened	SP1	Summary of Study Populations	IDSL	SAC
Demographic and Baseline Characteristics					
1.6.	ITT	DM1	Summary of Demographic and Baseline Characteristics	ICH E3, FDAAA, EudraCT Include: Baseline Eosinophil counts and Fitzpatrick skin type	SAC
1.7.	ITT	DM11	Summary of Age Ranges	EudraCT Note: Include Age categories: Adult (18 – 64 years), >=65 – 84 years and >=85 years.	SAC
1.8.	ITT	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT	SAC

Study Population Tables					
No.	**Population**	**IDSL/ Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Prior and Concomitant Medications					
1.9.	ITT	MH1	Summary of Past Medical Conditions	ICH E3	SAC
Exposure					
1.10.	Safety	POP_T1	Summary of Exposure to Study Treatment	ICH E3	SAC

12.9.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL/ Example Shell**	**Title**	**Programming Notes**	**Deliverable**
IGA					
2.1.	ITT	EFF_T1	Bayesian Posterior Probability for Comparison between Mepolizumab and Placebo	Note: Non-Responder imputation will be used	SAC
2.2.	ITT	EFF_T2	Number (%) of Participants in Each Category of the Investigator's Global Assessment Scale at Each Visit		SAC
2.3.	ITT	EFF_T3	Summary of Proportion of Participants with IGA Score of 0 or 1 and at Least a 2-Grade Improvement from Baseline at Each Visit	Note: Non-Responder imputation will be used	SAC
EASI					
2.4.	ITT	EFF_T4	Summary of Change from Baseline/Percent Change from Baseline in EASI Score at Each Visit	Note: CFB, %CFB in bylines	SAC
2.5.	ITT	EFF_T4	Summary of Change from Baseline/Percent Change from Baseline in EASI Score at Each Visit by Baseline Blood Eosinophil Count Quartiles	Note: Include Quartiles categories as <=Q1(x), >Q1(x) - <=Q2, >Q2(x) - <=Q3(x) and >Q3(x). Include all quartiles value(x)	SAC
2.6.	ITT	EFF_T5	Summary of Proportion of Participants with >=50% and >=75% Improvement in EASI Score from Baseline at Each Visit	Note: >=50%, >=75% improvement in bylines.	SAC
Patient Reported Outcomes					
2.7.	ITT	EFF_T4	Summary of Change from Baseline in Weekly Average of Daily Itch/pruritus NRS Score (based on Item #1 of Daily Sign and Symptom Severity Diary) at Each Visit	Includes Baseline values. Note: Mean change from baseline will be presented to only Week 4, 8, 12, 16 and 20	SAC

12.9.6. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Adverse Events (AEs)					
3.1.	Safety	AE1	Summary of All On-Treatment Adverse Events by System Organ Class and Preferred Term	ICH E3	SAC
3.2.	Safety	AE1	Summary of All Post-Treatment Adverse Events by System Organ Class and Preferred Term	ICH E3	SAC
3.3.	Safety	AE15	Summary of Common (>=3%) On-Treatment Non-Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences)	FDAAA, EudraCT	SAC
3.4.	Safety	AE1	Summary of Adverse Events Reported on the Day of Dosing by System Organ Class and Preferred Term		SAC
3.5.	Safety	AE1	Summary of On-Treatment Adverse Events by Highest Binding Antibody Result		SAC
Serious and Other Significant Adverse Events					
3.6.	Safety	AE16	Summary of On-Treatment Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences)	FDAA, EudraCT	SAC
3.7.	Safety	AE16	Summary of Post-Treatment Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences)	FDAA, EudraCT	SAC
3.8.	Safety	AE3	Summary of Fatal Serious Adverse Events by Overall Frequency		SAC
Adverse Events of Special Interest (AESI's)					
3.9.	Safety	SAF_T1	Summary of On-Treatment Adverse Events of Special Interest Reported by the Investigator as Meeting the Criteria for Anaphylaxis		SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.10.	Safety	SAF_T2	Summary Profile of On-Treatment Adverse Events Reported by the Investigator as Meeting the Criteria for Anaphylaxis	Produced only if more than one AESI reported in this category.	SAC
3.11.	Safety	SAF_T1	Summary of On-Treatment Adverse Events of Special Interest Reported by the Investigator as Systemic Reactions - Allergic (Type I Hypersensitivity) and Other Systemic		SAC
3.12.	Safety	SAF_T2	Summary Profile of On-Treatment Adverse Events Reported by the Investigator as Systemic Reactions - Allergic (Type I Hypersensitivity) and Other Systemic	Produced only if more than one AESI reported in this category.	SAC
3.13.	Safety	SAF_T1	Summary of On-Treatment Adverse Events of Special Interest Reported by the Investigator as Systemic Reactions - Allergic (Type I Hypersensitivity)		SAC
3.14.	Safety	SAF_T2	Summary Profile of On-Treatment Adverse Events Reported by the Investigator as Systemic Reactions - Allergic (Type I Hypersensitivity)	Produced only if more than one AESI reported in this category.	SAC
3.15.	Safety	SAF_T1	Summary of On-Treatment Adverse Events of Special Interest Reported by the Investigator as Systemic Reactions - Other Systemic		SAC
3.16.	Safety	SAF_T2	Summary Profile of On-Treatment Adverse Events Reported by the Investigator as Systemic Reactions - Other Systemic	Produced only if more than one AESI reported in this category.	SAC
3.17.	Safety	SAF_T1	Summary of On-Treatment Adverse Events of Special Interest Reported by the Investigator as Local Injection Site Reactions		SAC
3.18.	Safety	SAF_T2	Summary Profile of On-Treatment Adverse Events Reported by the Investigator as Local Injection Site Reactions	Produced only if more than one AESI reported in this category.	SAC
3.19.	Safety	SAF_T1	Summary of On-Treatment Adverse Events of Special Interest Categorised as Serious Cardiac, Vascular and Thromboembolic Events		SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.20.	Safety	SAF_T2	Summary Profile of On-Treatment Adverse Events of Special Interest Categorised as Serious Cardiac, Vascular and Thromboembolic Events	Produced only if more than one AESI reported in this category.	SAC
3.21.	Safety	SAF_T1	Summary of On-Treatment Adverse Events of Special Interest Categorised as Serious Ischemic Events		SAC
3.22.	Safety	SAF_T2	Summary Profile of On-Treatment Adverse Events of Special Interest Categorised as Serious Ischemic Events	Produced only if more than one AESI reported in this category.	SAC
3.23.	Safety	SAF_T1	Summary of On-Treatment Adverse Events of Special Interest Categorised as Malignancies		SAC
3.24.	Safety	SAF_T2	Summary Profile of On-Treatment Adverse Events of Special Interest Categorised as Malignancies	Produced only if more than one AESI reported in this category.	SAC
3.25.	Safety	SAF_T1	Summary of On-Treatment Adverse Events of Special Interest Categorised as Opportunistic Infections		SAC
3.26.	Safety	SAF_T2	Summary Profile of On-Treatment Adverse Events of Special Interest Categorised as Opportunistic Infections	Produced only if more than one AESI reported in this category.	SAC
Laboratory: Chemistry					
3.27.	Safety	LB1	Summary of Chemistry Changes from Baseline	ICH E3 Includes Baseline values.	SAC
3.28.	Safety	LB3	Summary of Chemistry Shifts from Baseline Relative to Normal Range		SAC
3.29.	Safety	LB3	Summary of Emergent Chemistry Results (Relative to the Potential Clinical Concern Range)	ICH E3	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Laboratory: Haematology					
3.30.	Safety	LB1	Summary of Haematology Changes from Baseline	ICH E3 Includes Baseline values.	SAC
3.31.	Safety	LB3	Summary of Haematology Shifts from Baseline Relative to Normal Range		SAC
3.32.	Safety	LB17	Summary of Emergent Haematology Results (Relative to the Potential Clinical Concern Range)	ICH E3	SAC
ECG					
3.33.	Safety	EG1	Summary of ECG Findings	The ECG findings to be summarized are the ECG interpretation, clinical significance of abnormal ECGs	SAC
3.34.	Safety	EG2	Summary of Change from Baseline in ECG Values by Visit	Includes Baseline values.	SAC
3.35.	Safety	EG10	Summary of Actual and Change from Baseline QTc(F) Values by Category	Category column will be replaced and created based on the information provided in the Section 8.4.1. For Anytime Post-Baseline, the highest post-baseline QTcF value and the change from baseline for this highest post-baseline QTc value is categorised	SAC
Vital Signs					
3.36.	Safety	VS1	Summary of Change from Baseline in Vital Signs	Includes Baseline values.	SAC
3.37.	Safety	VS3	Summary of Worst Case Vital Signs Results by PCI Criteria Post-Baseline Relative to Baseline		SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Immunogenicity					
3.38.	Safety	SAF_T3	Summary of Binding Antibody by Visit		SAC
3.39.	Safety	SAF_T4	Summary of Neutralising Antibody by Visit		SAC
3.40.	Safety	SAF_T5	Summary of Binding Antibody Assay Results: Highest Treatment Emergent Confirmatory Result Any Time Post Baseline		SAC

12.9.7. Safety Figures

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Laboratory					
3.1.	Safety	LIVER14	Scatter Plot of Maximum vs. Baseline for ALT	IDSL Note: Figure created as no liver events report, but such a plot may flag participants who were not reported.	SAC
3.2.	Safety	LIVER9	Scatter Plot of Maximum ALT vs. Maximum Total Bilirubin	IDSL	SAC

12.9.8. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
4.1.	PK	PKCT1	Summary of Plasma Mepolizumab Pharmacokinetic Concentration-Time Data		SAC

12.9.9. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
4.1.	PK	PK_F1	Scatter Plot of Individual Plasma Concentration Data by Participants' ADA Status	Note: Participants' ADA status is highest ADA result (Positive or Negative) in any post bassline visit.	SAC
4.2.	PK	PK_F1	Scatter Plot of Individual Plasma Concentration Data (with Mean ± SD)	Include Mean ± SD for each visit along with the individual plasma conc. data	SAC

12.9.10. Pharmacodynamic and Biomarker Tables

Pharmacodynamic and Biomarker: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Blood Eosinophil Counts					
5.1.	Safety	PD_T1	Summary of Blood Eosinophils Count at Each Visit	1. Include both absolute and ratio to baseline for log transformed blood eosinophil count.	SAC
5.2.	Safety	PD_T2	Summary of Mixed Model Repeated Measures (MMRM) Analysis for Blood Eosinophils Count		SAC

12.9.11. Pharmacodynamic and Biomarker Figures

Pharmacodynamic and Biomarker: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Blood Eosinophil Counts					
5.1.	Safety	PD_F1	Scatter Plot of Individual Absolute Blood Eosinophils Count by Participants' ADA status	Note: Participants' ADA status is highest ADA result (Positive or Negative) in any post bassline visit.	SAC
5.2.	Safety	PD_F2	Plot of Least Squares Geometric Means and 95% CI of Ratio to Baseline in Blood Eosinophil Count		SAC

12.9.12. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.	Screened	ES7	Listing of Reasons for Screen Failure	Journal Guidelines	SAC
2.	ITT	ES2	Listing of Reasons for Study Withdrawal	ICH E3	SAC
3.	ITT	SD2	Listing of Reasons for Study Treatment Discontinuation	ICH E3	SAC
4.	ITT	BL1	Listing of Participants for Whom the Treatment Blind was Broken	ICH E3	SAC
5.	ITT	TA1	Listing of Planned and Actual Treatments	IDSL	SAC
Protocol Deviations					
6.	ITT	DV2	Listing of Important Protocol Deviations	ICH E3	SAC
7.	ITT	IE3	Listing of Participants with Inclusion/Exclusion Criteria Deviations	ICH E3	SAC
Demographic and Baseline Characteristics					
8.	ITT	DM2	Listing of Demographic and Baseline Characteristics	ICH E3 Include Baseline Eosinophil Count and Fitzpatrick skin type	SAC
9.	ITT	DM9	Listing of Race	ICH E3	SAC
Prior and Concomitant Medications					
10.	ITT	CM3	Listing of Concomitant Medications	ICH E3	SAC
Exposure					
11.	Safety	EX3	Listing of Exposure Data	ICH E3	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Adverse Events					
12.	Safety	AE8	Listing of All Adverse Events	ICH E3	SAC
13.	Safety	AE7	Listing of Participant Numbers for Individual Adverse Events	ICH E3	SAC
14.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	SAC
15.	Safety	AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment		SAC
16.	Safety	AE8	Listing of Adverse Events Reported on the Day of Dosing		SAC
17.	Safety	AE8	Listing of All Adverse Events of Special Interest	Produced only if more than one AESI reported.	
All Laboratory					
18.	Safety	LB5	Listing of All Chemistry Laboratory Data for Participants with Any Value of Potential Clinical Importance	ICH E3	SAC
19.	Safety	LB5	Listing of All Haematology Laboratory Data for Participants with Any Value of Potential Clinical Importance	ICH E3	SAC
20.	Safety	LB14	Listing of Laboratory Data with Character Results		SAC
21.	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting		
22.	Safety	LIVER13	Listing of Subjects Meeting Hepatobiliary Laboratory Criteria Post-Baseline		
ECG					
23.	Safety	EG3	Listing of ECG Values (Participants with QTcF >500 msec or Increase > 60 msec from Baseline)		SAC
24.	Safety	EG5	Listing of Abnormal ECG Findings	IDSL	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Vital Signs					
25.	Safety	VS4	Listing of All Vital Signs Data for Participants with Any Value of Potential Clinical Importance	IDSL	SAC
Immunogenicity					
26.	Safety	IMM2	Listing of Immunogenicity Results	IDSL. Include columns for Screening Binding Assay, Confirmation Antibody Assay, Confirmation Assay Titre, Transient/Persistent, Neutralizing Antibody Assay	SAC

12.9.13. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
IGA					
27.	ITT	EFF_L1	Listing of Investigator's Global Assessment (IGA) Score	Note: Include Character result, Numeric score & CFB	SAC
EASI and %BSA					
28.	ITT	EFF_L2	Listing of Eczema Area and Severity Index (EASI) Score	Note: Include Character result, Numeric score, CFB & %CFB	SAC
29.	ITT	EFF_L4	Listing of Total Body Surface Area (%BSA)	Note: Include Numeric score & CFB	SAC
Patient-Reported Outcomes					
30.	ITT	EFF_L3	Listing of Weekly Average of Daily itch/ pruritus NRS score (based on Item #1 of Daily Sign and Symptom Severity Diary)	Note: Include Numeric score & CFB for all derived visits	SAC
31.	ITT	EFF_L4	Listing of Daily Sign and Symptom Severity Diary	Note: Include Numeric score	SAC
32.	ITT	EFF_L4	Listing of Patient Global Impression of Change Scores	Note: Severity of eczema symptoms and Severity of itch in by-lines. Note: Include Character result, Numeric score	SAC
33.	ITT	EFF_L4	Listing of Patient Global Impression of Severity Scores	Note: Include Character result, Numeric score & CFB	SAC
34.	ITT	EFF_L4	Listing of Clinician Global Impression of Change Scores	Note: Include Character result, Numeric score	SAC
PK					
35.	PK	PKCL1P	Listing of Plasma Mepolizumab Concentration Time Data		SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Blood Eosinophil Counts and Biomarkers					
36.	Safety	EFF_L4	Listing of Blood Eosinophil Counts	Include both absolute and ratio to baseline blood eosinophil count	
37.	Safety	N/A	Listing of Raw SAS Output for Mixed Model Repeated Measures (MMRM) Analysis for Blood Eosinophils Count		
38.	PD	EFF_L4	Listing of Serum Free and Total Serum IL-5 Levels		
39.	PD	EFF_L4	Listing of Serum Biomarker Endpoints		
40.	ITT	N/A	Listing of Raw SAS output of Bayesian Analysis of Response Rate in Investigator's Global Assessment (IGA) Score		

12.10. Appendix 10: Example Mock Shells for Data Displays

Example: POP_T1 Page 1 of n
Protocol: 205050
Population: Safety

Table 1.10
Summary of Exposure to Study Treatment

		Placebo SC (N=xx)	Mepolizumab 100mg SC (N=xx)
Treatments Administered	n	68	68
	Mean	11.6	12.7
	SD	3.30	1.33
	Median	13.0	13.0
	Min.	2	4
	Max.	14	14
Number of Treatments	1	0	0
	2	2 (3%)	0
	3	3 (4%)	0
	4	3 (4%)	1 (1%)
Number of Days on Treatment	n	68	68
	Mean	330.8	357.2
	SD	91.43	37.39
	Median	365.0	365.0
	Min.	57	114
	Max.	394	392

Note: Number of Days on Treatment = (Treatment Stop Date – Treatment Start Date) + another 28 days inclusive.

Example: EFF_T1
Protocol: 205050
Population: Intent-to-Treat

Table 2.1

Bayesian Posterior Probability for Comparison between Mepolizumab and Placebo

Visit	Treatment	n	Posterior Mean Response Rate (80% Cred Int)	Posterior Median Response Rate (80% Cred Int)	Posterior Mean Difference (80% Cred Int)	Posterior Probability of Response Rate ≥ 40%	Posterior Probability of difference of Response Rate ≥ 15%
Week 16	Mepolizumab 100 mg SC	xx	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)	xx.xx	xx.xx
	Placebo SC	xx	xx.x x (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)			

Note: A Responder is defined as a subject who has an IGA score of 0 or 1 and a minimum 2-grade improvement from baseline. If a subject withdraws early from the study the due to lack of efficacy or disease progression, then all weeks after withdrawal they are assigned to be a non-responder.

Note: 0=Clear; 1=Almost Clear; 2=Mild; 3=Moderate; 4=Severe.

Example: EFF_T2
Protocol: 205050
Population: Intent-to-Treat

Table 2.2
Number (%) of Subjects in Each Category of the Investigator's Global Assessment Scale at Each Visit

Visit	Category	Placebo SC (N=XX)	Mepolizumab 100 mg SC (N=XX)
Day 1			
	n	XX	XX
	Clear	XX (XX%)	XX (XX%)
	Almost Clear	XX (XX%)	XX (XX%)
	Mild	XX (XX%)	XX (XX%)
	Moderate	XX (XX%)	XX (XX%)
	Severe	XX (XX%)	XX (XX%)

Programming note: Repeat for all study visits

Example: EFF_T3
Protocol: 205050
Population: Intent-to-Treat

Table 2.3
Summary of Proportion of Subjects with an IGA Score of 0 or 1 and at Least a 2-Grade Improvement from Baseline at Each Visit

Visit	IGA score of 0 or 1 and at least a 2-grade improvement	Placebo SC (N=XX)	Mepolizumab 100mg SC (N=XX)	Proportions Difference	90% CI for the Proportions Difference
Week 4	n	XX	XX		
	Yes	XX (XX%)	XX (XX%)	XX%	(XX.X%, XX.X%)
	No	XX (XX%)	XX (XX%)		

Note: A Responder is defined as a subject who has an IGA score of 0 or 1 and a minimum 2-grade improvement from baseline. If a subject withdraws early from the study the due to lack of efficacy or disease progression, then all weeks after withdrawal they are assigned to be a non-responder.
Note: Day 1 is considered as baseline.
Note: 0=Clear; 1=Almost Clear; 2=Mild; 3=Moderate; 4=Severe.
Programming note: Repeat for all available visits

Example: EFF_T4
Protocol: 205050
Population: Intent-to-Treat

Table 2.4
Summary of Change from Baseline/Percent Change from Baseline in EASI Score at Each Visit

Summary: Change from Baseline

Visit		Placebo SC (N=XX)	Mepolizumab 100mg SC (N=XX)
Day 1	n	XX	XX
	Mean	x.x	x.x
	SD	X.XX	X.XX
	Median	x.x	x.x
	Min.	X	X
	Max.	X	X
Week 4	n	XX	XX
	Mean	x.x	x.x
	SD	X.XX	X.XX
	Median	x.x	x.x
	Min.	X	X
	Max.	X	X

Summary: Percentage Change from Baseline

……[Format as Change from Baseline]

Note: Day 1 is considered as baseline and summarized for absolute value.
Programming note: Repeat for all available visits and include percent change from baseline

Example: EFF_T5
Protocol: 205050
Population: Intent-to-Treat

Table 2.6
Summary of Proportion of Subjects with >=50% and >=75% Improvement in EASI Score from Baseline at Each Visit

Visit	Improvement in EASI Score from baseline	Placebo SC (N=XX)	Mepolizumab 100mg SC (N=XX)	Proportions Difference	90% CI for the Proportions Difference
Week 4	n	XX	XX		
	>=50% improvement	XX (XX%)	XX (XX%)	XX%	(XX.X%, XX.X%)
	>=75% improvement	XX (XX%)	XX (XX%)	XX%	(XX.X%, XX.X%)

Example: SAF_T1 Page 1 of n
Protocol: 205050
Population: Intent-to-Treat

Table 3.9
Summary of On-Treatment Adverse Events of Special Interest Reported by the Investigator as Meeting the Criteria for Anaphylaxis

	Placebo SC (N=XX)	Mepolizumab 100mg SC (N=XX)
Number of Subjects with Any Event	xx (xx%)	xx (xx%)
Hypersensitivity		
Number of Subjects with Any Event	XX (XX%)	XX (XX%)
Facial Paralysis	XX (XX%)	XX (XX%)
Flushing	XX (XX%)	XX (XX%)
Injection related reaction	XX (XX%)	XX (XX%)
Rash	XX (XX%)	XX (XX%)
Other Systemic Reactions		
Number of Subjects with Any Event	XX (XX%)	XX (XX%)
Facial Paralysis	XX (XX%)	XX (XX%)
Flushing	XX (XX%)	XX (XX%)
Injection related reaction	XX (XX%)	XX (XX%)
Rash	XX (XX%)	XX (XX%)

Example: SAF_T2
Protocol: 205050
Population: Safety

Table 3.10
Summary Profile of On-Treatment Adverse Events Reported by the Investigator as Meeting the Criteria for Anaphylaxis

	Placebo (N=xx)	Mepolizumab 100 mg SC (N=xx)
All Events		
>=1 event [1]	3/2 (3%)	5/5 (7%)
1 event	1 (1%)	5 (7%)
2 events	1 (1%)	0
3 events	0	0
>=4 events	0	0
Serious Events		
>=1 event [1]	1/1 (1%)	0
Events considered related to Investigational Product		
>=1 event [1]	1/1 (1%)	1/1 (1%)
Intensity [1]		
Mild	0	4/4 (6%)
Moderate	2/2 (3%)	1/1 (1%)
Severe	1/1 (1%)	0
Outcome [1]		
Recovered/Resolved	3/2 (3%)	5/5 (7%)
Recovering/Resolving	0	0
Not Recovered/Not Resolved	0	0

Recovered/Resolved With Sequelae	0	0
Fatal	0	0
Action Taken [1]		
Drug withdrawn	0	0
Dose reduced	0	0
Dose increased	0	0
Dose not changed	3/2 (3%)	5/5 (7%)
Dose interrupted	0	0
Not applicable	0	0
No. doses prior to event [1]		
1	0	0
2	0	1/1 (1%)
3	0	0
4	0	1/1 (1%)
No. doses prior to first event		
1	0	0
2	0	1 (1%)
3	0	0
4	0	1 (1%)

[1] Information presented as number of events / number (%) participants with at least one event. Subjects may be counted in more than one row.

Example: SAF_T3
Protocol: 205050
Population: Safety

Table 3.38
Summary of Binding Antibody by Visit

Visit	Assay Result		Placebo (N=68)	Mepolizumab 100 mg SC (N=68)
Baseline	n		xx	xx
	Negative		xx (xx%)	xx (xx%)
	Positive		xx (xx%)	xx (xx%)
	Titer Value	Median	32.0	32.0
		Min.	32	32
		Max.	32	32
Week 4	n		xx	xx
	Negative		xx (xx%)	xx (xx%)
	Positive		xx (xx%)	xx (xx%)
	Transient Positive		xx (xx%)	xx (xx%)
	Persistent Positive		xx (xx%)	xx (xx%)
	Titer Value	Median	32.0	32.0
		Min.	32	32
		Max.	32	32
Anytime Post Baseline	n		xx	xx
	Negative		xx (xx%)	xx (xx%)
	Positive		xx (xx%)	xx (xx%)
	Transient Positive		xx (xx%)	xx (xx%)

Persistent Positive		xx (xx%)	xx (xx%)
Titer Value	Median	32.0	32.0
	Min.	32	32
	Max.	32	32

Note: The values shown at the anytime post baseline visit are based on each participants highest post baseline titer.
Any time post baseline would be Positive for a participants who had Negative and Positive post baseline results

Example: SAF_T4
Protocol: 205050
Population: Safety

Table 3.39
Summary of Neutralising Antibody by Visit

Visit	Assay Result	Placebo (N=xx)	Mepolizumab 100 mg SC (N=xx)
Baseline	n	xx	xx
	Negative	xx (xx%)	xx (xx%)
	Positive	xx (xx%)	xx (xx%)
Week 4	n	xx	xx
	Negative	xx (xx%)	xx (xx%)
	Positive	xx (xx%)	xx (xx%)
Anytime Post Baseline	n	xx	xx
	Negative	xx (xx%)	xx (xx%)
	Positive	xx (xx%)	xx (xx%)

Note: NAb assay result only presented for participant with positive ADA assay.
Any time post baseline would be Positive for a participant who had both Negative and Positive post baseline results.

Example: SAF_T5
Protocol: 205050
Population: Safety

Table 3.40
Summary of Binding Antibody Assay Results: Highest Treatment Emergent Confirmatory Result
Any Time Post Baseline

Assay Result	Placebo (N=xx)	Mepolizumab 100 mg SC (N=xx)
n	xx	xx
Negative	xx (xx%)	xx (xx%)
Positive	xx (xx%)	xx (xx%)
Transient Positive	xx (xx%)	xx (xx%)
Persistent Positive	xx (xx%)	xx (xx%)
Titer Value		
Median	32.0	32.0
Min.	32	32
Max.	32	32

Note: Includes only results from subjects who do not have a positive ADA assay prior to the first dose of investigational product.

Example: PD_T1
Protocol: 205050
Population: Intent-to-Treat

Table 5.1
Summary of Blood Eosinophil Count at Each Visit

Visit			Placebo SC (N=68)	Mepolizumab 100 mg SC (N=68)
Baseline	Blood Eosinophils (10^9/L)	n	68	68
		Geo Mean	0.172	0.177
		Std Logs	1.3522	1.2890
		Median	0.215	0.190
		Min.	0.00	0.01
		Max.	4.45	6.72
Week 4	Blood Eosinophils (10^9/L)	n	66	66
		Geo Mean	0.141	0.035
		Std Logs	1.4972	0.9999
		Median	0.195	0.040
		Min.	0.00	0.00
		Max.	3.35	1.56
	Blood Eosinophils Ratio to Baseline	n	66	66
		Geo Mean	0.796	0.189
		Std Logs	1.2976	1.1936
		Median	0.964	0.185
		Min.	0.00	0.00
		Max.	22.00	4.00

Note: Data were log transformed.
Note: Where a result of zero was recorded, a small value (i.e. minimum all non-missing results/2) was added prior to log transformation

Example: PD_T2
Protocol: 205050
Population: Safety

Table 5.2
Summary of Mixed Model Repeated Measures (MMRM) Analysis for Blood Eosinophils Count

Visit	Statistic	Placebo SC N=xx	Mepolizumab 100 mg SC N=xx
Week 4	n	xx	xx
	LS Geometric Mean (SE)	x.xx (xx.xxx)	x.xx (xx.xxx)
	LS Geometric Mean Ratio to Baseline (SE)	x.xx (xx.xxx)	x.xx (xx.xxx)
	95% Confidence Interval	(x.xx, x.xx)	(x.xx, x.xx)
	Treatment Ratio		x.xx
	95% Confidence Interval		(x.xx, x.xx)
Week 8	n	xx	xx
	LS Geometric Mean (SE)	x.xx (xx.xxx)	x.xx (xx.xxx)
	LS Geometric Mean Ratio to Baseline (SE)	x.xx(xx.xxx)	x.xx (xx.xxx)
	95% Confidence Interval	(x.xx, x.xx)	(x.xx, x.xx)
	Treatment Ratio		x.xx
	95% Confidence Interval		(x.xx, x.xx)

Note: Treatment Ratio (Mepolizumab/Placebo) and 95% Confidence Intervals for Ratio to Placebo are obtained from MMRM model, with fixed categorical effects of Treatment, Visit, and Treatment-By-Visit Interaction and fixed continuous covariates of Baseline. 'XX' covariance structure was used.
Note: n is the number of participants with non-missing data at that visit.

Example: EFF_L1
Protocol: 205050
Population: Intent-to-Treat

Listing 24
Listing of Investigator's Global Assessment(IGA) Score

Treatment	Site ID./ Subj.	Visit/ Analysis Visit	Date/ Study Day	IGA Character result	IGA Score	Change from Baseline score	Study Treatment Period	Follow-Up Period	Relapsed (Y/N) [1]
	XXX/ XXX	WEEK 2/		Moderate					
	XXX/ XXX								

[1] Participants who have an IGA score of 3 or 4 after achieving an IGA score of 0 or 1 and at least a 2-grade improvement during the Treatment and Follow-up Periods.

Example: EFF_L2
Protocol: 205050
Population: Intent-to-Treat

Listing 25
Listing of Eczema Area and Severity Index (EASI) Score

Treatment	Site ID./ Subj.	Visit/ Analysis Visit	Date/ Study Day	EASI Score	Change from Baseline Score	Study Treatment Period	Follow-Up Period	Relapsed(Y/N) [1]
	XXX/ XXX	WEEK 2/						
	XXX/ XXX							

[1]: Participants who have an increase in EASI score of >=25% from baseline during the Treatment and Follow-up Periods

Example: EFF_L3
Protocol: 205050
Population: Intent-to-Treat

Listing 27

Listing of Weekly Average of Daily Itch/pruritus NRS score (based on Item #1 of Daily Sign and Symptom Severity Diary)

Treatment	Site ID./ Subj.	Visit/ Analysis Visit	Numeric Score	Change from Baseline Score
	XXX/ XXX	WEEK 2/		
	XXX/ XXX			

Example: EFF_L4
Protocol: 205050 Page 1 of x
Population: Intent-to-Treat

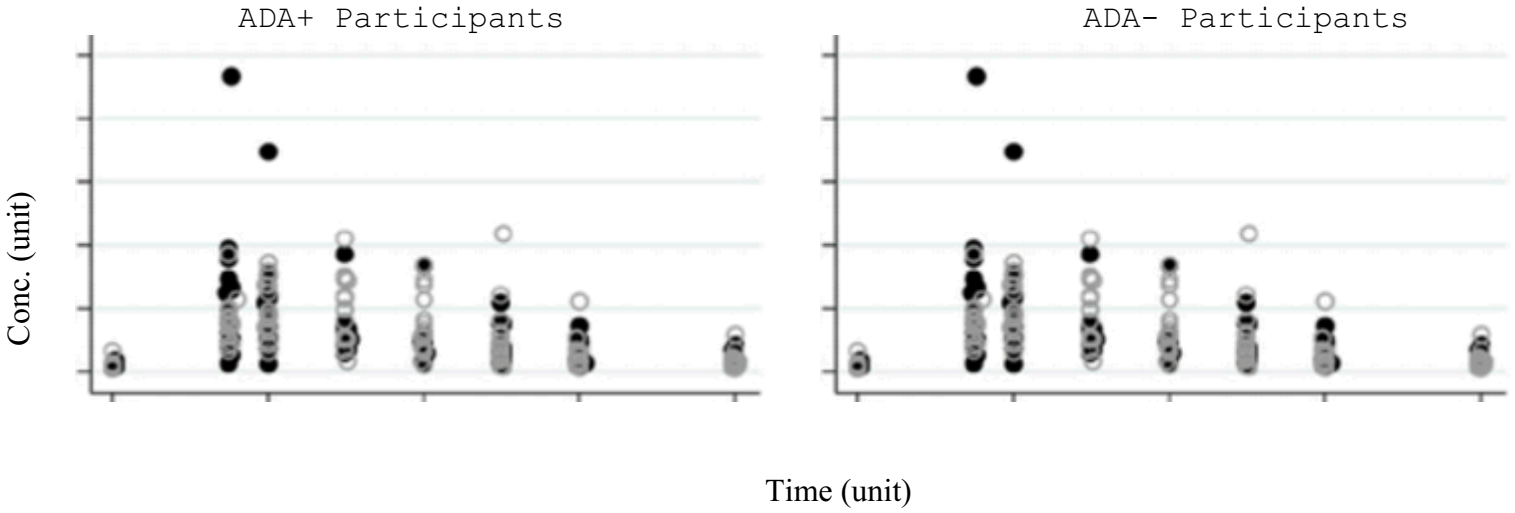
Listing of xxxxxx

Treatment	Site ID./ Subj.	Visit/ Analysis Visit [optional]	Date/ Study Day	Character result [optional]	Numeric Score	Change from Baseline [optional]
	XXX/ XXX	WEEK 2/				
	XXX/ XXX					

Programming Note: Include optional columns as required.

Example: PK_F1/PD_F1
Protocol: 205050
Population: Intent-to-Treat

Figure 4.1
Scatter plot of Individual Plasma Concentration Data by Participants' ADA Status



Example: PD_F2
Protocol: 205050
Population: Intent-to-Treat

Figure 5.2
Plot of Least Squares Geometric Means and 95% CI of Ratio to Baseline in Blood Eosinophil Count