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Description:

The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for the Long-term Access Programme (LAP) for mepolizumab in EGPA. The LAP comprises a clinical trial (MEA116841) and compassionate use programme (201607). Planned outputs also include periodic interim analyses conducted after the effective date of this RAP, as necessary.

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses and planned outputs to be included in the Clinical Study Report for the Long-term Access Programme (LAP) for mepolizumab in EGPA. The LAP comprises a clinical trial (MEA116841) and compassionate use programme (201607). This document also describes the planned outputs to be included in periodic interim analyses, conducted after the effective date of this RAP, as appropriate

This RAP is based on MEA116841 study protocol amendment 4 issued 18-Jun-2019 (GlaxoSmithKline Document Number 2014N201870_04) and has been amended following the previous RAP version which has been used to provide the analyses required for the previous Interim Clinical Study Report (ICSRs).

The clinical data base for the LAP consists of the following subjects:

- Subjects recruited into study MEA116841
- Subjects recruited as part of the named patient supply guidance program 201607

Available data from the above subjects will be included in the analyses specified in this RAP. Combined summaries will be produced from the clinical trial data base for MEA116841 and the NPS guidance program.

1.1. RAP Amendments

All revisions since the previous approved RAP (dated 26-Sep-2016) are listed below:

RAP Section	Amendment Details
All	Formatting changes to fit RAP_Template_Master_v2 (8-Aug-2017)
3.1 Interim Analyses	Details of previous interim analysis (5-Sep-2016 cut-off date) were added
4.1 Protocol Deviations	Reference added to updated PDMP
7.1 Safety Analyses	Added text providing additional information regarding adverse event reporting for MEA116841 and 201607
9.7.4 Study Population Tables	• Removed “Summary of Reasons for Screen and Run-In Failure“ (Rationale: there was only one occurrence and these data are included in the listings) • Removed “Summary of Inclusion/Exclusion Criteria” (Rationale: there was only one occurrence and these data are included in the listings) • Added “Summary of Age Ranges” (Required as per revised RAP template) • Added “Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences)” (Required for disclosure purposes).

RAP Section	Amendment Details
	• Added “Summary of Non-Serious Drug-Related Adverse Events by Overall Frequency” (Required for Plain language Summaries) • Added “Summary of Non-Serious Drug-Related Adverse Events by Overall Frequency” (Required for Plain language Summaries)

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

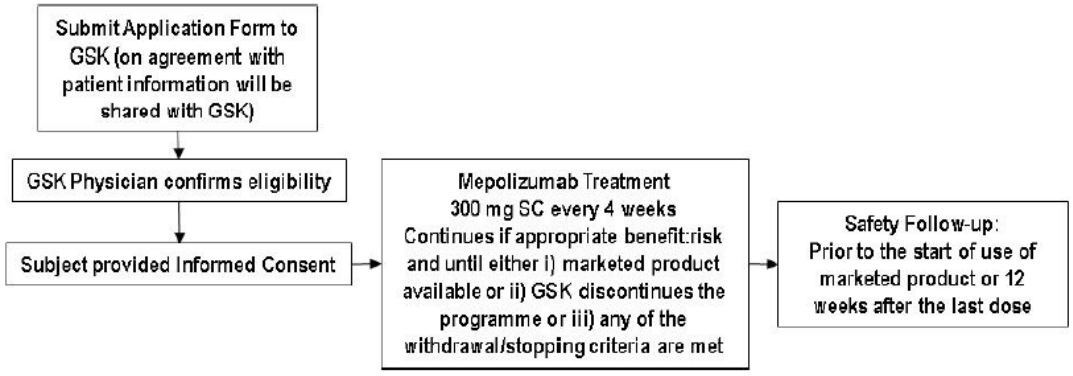
There were no changes or deviations to the originally planned statistical analysis specified in the protocol.

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

Objective	Endpoints
The objective of this protocol is to provide a mechanism to supply mepolizumab on an individual subject basis to eligible subjects who previously participated in GSK sponsored study MEA115921.	N/A

2.3. Study Design

Overview of Study Design and Key Features



Design Features	See figure above.
Dosing	Eligible subjects will receive subcutaneously administered mepolizumab at a dose of 300 mg SC every 4 weeks.
Treatment Assignment	All eligible subjects will receive mepolizumab as described above.

2.4. Statistical Hypotheses / Statistical Analyses

No statistical hypotheses are defined for this study.

3. PLANNED ANALYSES

3.1. Interim Analyses

A summary of integrated safety data from MEA116841 and 201607 (compassionate use programme) was conducted to support mepolizumab EGPA submissions in the US and Japan, using a cut-off date of 05-SEP-2016 (GlaxoSmithKline Document Number: 2017N320079_00).

Further interim analyses may be conducted, as required.

This RAP contains details of analyses proposed for future interim analyses as well as the final study report. Access to the results from such interim analyses will not be confidential. Specifically the results will be provided to the study team and GSK governance boards, and may be provided to external investigators and to regulatory authorities.

3.2. Final Analyses

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

1. All participants have completed the study as defined in the protocol
2. All required database cleaning activities have been completed and final database release (DBR) and database freeze (DBF) has been declared by Data Management.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Subjects Enrolled	Comprises all subjects enrolled and for whom a record exists on the study database. This population will be used for summarising reasons for screen and run-in failures.	Study Population
Safety	Comprise of all subjects who receive at least one dose of mepolizumab	• Study Population • Safety

4.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, failure to report pregnancy and SAEs and informed consent) will be summarised and listed.

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan [version 5.0, 05-June-2019].

- Data will be reviewed prior to freezing the database to ensure all important deviations are captured and categorised on the protocol deviations dataset.

- This dataset will be the basis for the summaries and listings of protocol deviations.

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

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment and Subgroup Display Descriptors

Summaries will be presented for all subjects receiving open-label mepolizumab. In addition, summaries will also be presented by the actual treatment the participant received in the randomised double-blind study (MEA115921).

Treatment group descriptors will be assigned as follows:

Treatment Group Descriptions			
RandAll NG from Study MEA115921		**Data Displays for Reporting**	
Code	**Description**	**Description**	**Order [1]**
P	Placebo	300mg SC Prev. Placebo	1
A	Mepolizumab 300mg SC	300mg SC Prev. Mepo	2
N/A	N/A	300mg SC Total	3

5.2. Examination of Subgroups

The following subgroups are defined for this study:

Subgroups
Age group: • <65 years • ≥65 years
Sex • Male • Female
Race • African American/African Heritage • White • Asian • Other

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
9.2	Appendix 2: Study Phases and Treatment Emergent Adverse Events
9.3	Appendix 3: Data Display Standards & Handling Conventions
9.4	Appendix 4: Derived and Transformed Data
9.5	Appendix 5: Reporting Standards for Missing Data

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the Safety population.

Study population analyses including analyses of subject's disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, and exposure and treatment compliance will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 7: List of Data Displays.

7. SAFETY ANALYSES

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

The LAP comprises a clinical trial (MEA116841) and compassionate use programme (201607) restricted to subjects who participated in MEA115921. The compassionate use programme (CUP) was conducted under a guidance document which mirrored the objectives of MEA116841. Since 201607 was run as a CUP, the treating physician was the responsible party. Per local legal requirements, serious adverse event reporting was required at a minimum. Furthermore, GSK did not monitor CUP 201607, and therefore verification that all non-serious adverse events (AEs) were reported is not possible.

For this reason, summaries of adverse events are reported separately for MEA116841 and 201607, with the exception of serious adverse events, which are additionally reported using combined MEA116841 and 201607 data.

7.1. Adverse Events

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) coding dictionary. Classification of an AE as pre-, on- or post-treatment will be made with reference to the study treatment start and stop date/time and the AE onset date/time. If the AE onset date is missing or partial then the AE will be considered on-treatment unless there is evidence to the contrary (e.g. the month of the onset date is present and is less than the month of the first dose of study medication). AEs with onset up to 4 weeks after the last dose of treatment will be considered on-treatment. AEs with onset after this period will be considered post-treatment but will be assigned to the treatment previously received.

Any SAEs for screen failures, run-in failures or subjects who were enrolled but did not receive treatment will be classified as pre-treatment SAEs.

The most frequent on-treatment AEs will be defined as AEs with frequency ≥3% in any treatment group.

7.2. Adverse Events of Special Interest

The following Adverse Events of Special Interest in mepolizumab clinical development have been defined:

- Systemic Allergic/Hypersensitivity and Non-allergic Reactions
- Local injection site reactions
- Alteration in immune response (infections)
- Alteration in immune response (malignancies)
- Alteration in cardiovascular safety
- Immunogenicity

The methods by which these events will be identified are detailed in the Program Safety Analysis Plan for Mepolizumab (PSAP), version 5 (effective 1-Apr-2019), Section 10.3.2

The details of the planned displays are provided in Appendix 7: List of Data Displays.

7.3. Other Safety Analyses

Details of listings of corticosteroid usage are provided in Appendix 7: List of Data Displays.

8. REFERENCES

- GlaxoSmithKline Document Number 2014N201870_04 Study ID MEA116841. Mepolizumab Long-term Access Programme for Subjects who Participated in Study MEA115921 (Placebo-controlled Study of Mepolizumab in the Treatment of Eosinophilic Granulomatosis with Polyangiitis in Subjects Receiving Standard-of-care Therapy). Protocol Amendment 4, Effective Date 18-Jun-2019.
- GlaxoSmithKline Document Number 2017N320079_00. Mepolizumab Long-term Access Programme for Subjects who Participated in Study MEA115921 (Placebo-controlled Study of Mepolizumab in the Treatment of Eosinophilic Granulomatosis with Polyangiitis in Subjects Receiving Standard-of-care Therapy). Interim Clinical Study Report, Effective 12-Jun-2017
- Program Safety Analysis Plan for Mepolizumab (SB240563) (PSAP). Version 5, Effective 1-April 2019. Author: Bhabita Mayer.

9. APPENDICES

9.1. Appendix 1: Schedule of Activities

9.1.1. Protocol Defined Schedule of Events

Visits and Assessments	Screening (up to 4 weeks)	Baseline	Week 4 (±7 days)	Week 8 (±7 days)	Week 12 (±7 days)	Week 16 (±7 days)	Week 20 (±7 days)	Week 24 (±7 days)	Every 4 week treatment cycle/assessments repeated until End of Treatment	Early withdrawal[3]	End of Treatment[3]/ Follow-up (12 weeks post-last dose)
Application Form sent to GSK for approval	X										
Written Informed Consent	X										
Demography and CV risk assessment	X										
Eligibility assessment: inclusion & exclusion criteria review	X										
Baseline information		X									
Dosing with mepolizumab[1,2]		X	X	X	X	X	X	X			
Corticosteroid use	X	X	X	X	X	X	X	X		X	X
AE/SAE review	X	X	X	X	X	X	X	X		X	X
Urine pregnancy test (FCBP)	X	X	X	X	X	X	X	X		X	X
Documentation of Benefit:risk evaluation to support continued supply of mepolizumab[1]	X	X			X			X			

1. The treating physician should make a benefit:risk evaluation to confirm continued treatment with mepolizumab is appropriate prior to each administration. This will be documented every 12 weeks to support continued supply. Note: it is expected that the treating physician will monitor subjects as per standard-of-care therapy (including any requirements for blood and urine tests).
2. Safety monitoring of subjects is required during SC administration and for 1 hour after the end of the injections for the first three administrations, i.e., at baseline, and Weeks 4 and 8. From Week 12 onwards, subjects can be monitored following mepolizumab administration in accordance with standard of care at the site.
3. See Section 5.3

9.2. Appendix 2: Study Phases and Treatment Emergent Adverse Events

9.2.1. Study Phases

Treatment State	Definition
Pre-Treatment	AE Start Date/Time < Study Treatment Start Date/Time
On-Treatment	Study Treatment Start Date/Time ≤ AE Start Date/Time ≤ Study Treatment Stop Date + 28 days
Post-Treatment	AE Start Date > Study Treatment Stop Date + 28 days

NOTES:

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

9.3. Appendix 3: Data Display Standards & Handling Conventions

9.3.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	CCI [redacted]
HARP Compound	
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 (ADC1/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.	

9.3.2. 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
• Do not include subject level listings in the main body of the GSK Clinical Study Report. All subject level listings should be located in the modular appendices as ICH or non-ICH listings

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, but may be adjusted to a clinically interpretable number of DPs.
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 Visits
• Unscheduled or unplanned readings will be presented within the subject's listings. • Visits outside the protocol defined time-windows (ie. recorded as protocol deviations) will be included in listings but omitted from figures, summaries and statistical analyses.

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.	

9.4. Appendix 4: Derived and Transformed Data

9.4.1. General

Study Day

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

9.4.2. 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. • If there are any treatment breaks during the study, exposure data will be adjusted accordingly.

9.4.3. Safety

Adverse Events
Drug Related AEs
AEs with relationship marked 'YES'.
AEs Leading to Permanent Discontinuation from Study Treatment or Withdrawal from the Study
AEs with action marked "Study treatment withdrawn" or withdrawn from study status marked "YES", or a response to either of these questions is missing.
AEs on Day of Dosing
AEs with an onset date equal to a study treatment dosing date and an onset time on or after the study treatment dosing time.
AE Time Since First Dose

• If AE onset time is missing, calculate in days as follows:-
  o If AE start date < Date of first dose of study treatment then
  Time since first dose = AE start date - Date of first dose of study treatment
  o If AE start date ≥ Date of first dose of study treatment then
  Time since first dose = AE start date – Date of first dose of study treatment +1
  o Missing if AE start date or date of first dose of study treatment is missing.
• If AE onset time is present, calculate in days, hours, minutes as
  Time since first dose = AE start date/time – Date/time of first dose of study treatment

AE Duration (Days)
• If AE onset time is missing, calculate in days as AE end date – AE start date + 1 • If AE onset time is present, calculate in days, hours and minutes as AE end date/time – AE start date/time • Missing if AE start date or end date is missing.
AEs of Special Interest
• See Section 7.2.

9.5. Appendix 5: Reporting Standards for Missing Data

9.5.1. Premature Withdrawals

Element	Reporting Detail
General	All available data from subjects in the Safety population who withdrew from mepolizumab will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

9.5.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument : ○ These data will be indicated by the use of a “blank” in 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.

9.5.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
Adverse Events	• Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events with be missing. • 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 2: Treatment States and Phases. ○ 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. • The recorded partial date will be displayed in listings.
Concomitant medications	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month ○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

9.6. Appendix 6: Abbreviations & Trade Marks

9.6.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AESI	Adverse Event of Special Interest
A&R	Analysis and Reporting
CDISC	Clinical Data Interchange Standards Consortium
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
CVT	Cardiac, Vascular and Thromboembolic
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Record Form
EGPA	Eosinophilic Granulomatosis with Polyangiitis
FCBP	Female of Childbearing Potential
IA	Interim Analysis
ICH	International Conference on Harmonisation
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
IP	Investigational Product
GSK	Glaxo SmithKline
GUI	Guidance
LAP	Long-term Access Programme
LOC	Last Observation Carries Forward
MedDRA	Medical Dictionary for Regulatory Activities
OSL	Operations and Science Lead
PCI	Potential Clinical Importance
PDMP	Protocol Deviation Management Plan
PP	Per Protocol
QC	Quality Control
RAP	Reporting & Analysis Plan
SAC	Statistical Analysis Complete
SDTM	Study Data Tabulation Model
SMQ	Standardised MedDRA Queries
SOP	Standard Operation Procedure
TA	Therapeutic Area
TFL	Tables, Figures & Listings

9.6.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
None

Trademarks not owned by the GlaxoSmithKline Group of Companies
Sas

9.7. Appendix 7: List of Data Displays

9.7.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.n	1.1 to 1.n
Safety	3.1 to 3.n	3.1 to 3.n
Section	**Listings**	
ICH Listings	1 to x	

9.7.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln

NOTES:

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

9.7.3. Deliverables

Delivery [1]	Description
IA SAC	Interim Analysis SAC (as appropriate)
SAC	Final SAC

9.7.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Safety	ES1	Summary of Subject Disposition	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC
1.2.	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC
1.3.	All Subjects Enrolled	NS1	Summary of Number of Participant by Country and Site ID	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC
Protocol Deviation					
1.4.	Safety	DV1	Summary of Important Protocol Deviations	• MEA116841	IA , SAC
Population Analysed					
1.5.	All Subjects Enrolled	mid_mepo_egpa_lap /interim1 Table 1.1	Summary of Study Populations	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC
Demographic and Baseline Characteristics					
1.6.	Safety	DM1	Summary of Demographic Characteristics	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.7.	All Subjects Enrolled	DM11	Summary of Age Ranges	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC
1.8.	Safety	DM5	Summary of Race and Racial Combinations	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC
1.9.	Safety	mid_mepo_egpa_lap /interim1 Table 1.10	Summary of Race and Racial Combinations Details	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC
1.10.	Safety	mid_mepo_egpa_lap /interim1 Table 1.11	Summary of Cardiovascular Assessments – Screening Questions	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC
1.11.	Safety	mid_mepo_egpa_lap /interim1 Table 1.12	Summary of Cardiovascular Assessments – Family History	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC
1.12.	Safety	mid_mepo_egpa_lap /interim1 Table 1.13	Summary of Oral Corticosteroid Therapy Taken Before the Treatment Period	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC
1.13.	Safety	mid_mepo_egpa_lap /interim1 Table 1.14	Summary of Oral Corticosteroid Therapy Taken During the Treatment Period	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC

9.7.5. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure					
3.1.	Safety	mid_mepo_egpa_lap /interim1 Table 3.1	Summary of Exposure to Study Treatment	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC
3.2.	Safety	mid_mepo_egpa_lap /interim1 Table 3.2	Summary of Number of Treatment Administered	• MEA116841 • 201607 • MEA116841 + 201607	IA , SAC
Adverse Events (AEs)					
3.3.	Safety	AE1	Summary of On-Treatment Adverse Events by System Organ Class and Preferred Term	• MEA116841 • 201607	IA , SAC
3.4.	Safety	AE1	Summary of Post-Treatment Adverse Events by System Organ Class and Preferred Term	• MEA116841 • 201607	IA , SAC
3.5.	Safety	AE3	Summary of Common (>=3%) Adverse Events by Preferred Term	• MEA116841 • 201607	IA , SAC
3.6.	Safety	AE1	Summary All Drug-Related Adverse Events by System Organ Class and Preferred Term	• MEA116841 • 201607As 3.1 notes	IA , SAC
3.7.	Safety	AE3	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by Preferred Term	• MEA116841 • 201607For studies with few events/participants, listing is sufficient.	IA , SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.8.	Safety	AE15	Summary of Common (>=3%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and Occurrences)	• MEA116841 • 201607Common' to be defined by study/project team. For studies with very few events/participants, listing is sufficient: discuss this option with your disclosure representative.	IA , SAC
3.9.	Safety	AE5A	Summary of On-Treatment Adverse Events by System Organ Class and Preferred Term and Maximum Intensity	• MEA116841 • 201607Common' to be defined by study/project team. For studies with very few events/participants, listing is sufficient: discuss this option with your disclosure representative.	IA , SAC
Serious and Other Significant Adverse Events					
3.10.	Safety	AE1	Summary of Pre-Treatment Serious Adverse Events by System Organ Class and Preferred Term	• MEA116841 • 201607For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative. • MEA116841 + 201607	IA , SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.11.	Safety	AE1	Summary of On-Treatment Serious Adverse Events by System Organ Class and Preferred Term	• MEA116841 • 201607For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative. • MEA116841 + 201607	IA , SAC
3.12.	Safety	AE1	Summary of Post-Treatment Serious Adverse Events by System Organ Class and Preferred Term	• MEA116841 • 201607For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative. • MEA116841 + 201607	IA , SAC
3.13.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences)	Required for data disclosure • MEA116841 • 201607For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative. • MEA116841 + 201607	IA , SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.14.	Safety	AE1	Summary of On-Treatment Non-Fatal Serious Adverse Events by System Organ Class and Preferred Term	• MEA116841 • 201607For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative. • MEA116841 + 201607	IA , SAC
3.15.	Safety	AE1	Summary of Fatal Serious Adverse Events by System Organ Class and Preferred Term	• MEA116841 • 201607For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative. • MEA116841 + 201607	IA , SAC
3.16.	Safety	AE1	Summary of Drug-Related Non-Fatal Serious Adverse Events by System Organ Class and Preferred Term	• MEA116841 • 201607For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative. • MEA116841 + 201607	IA , SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.17.	Safety	AE1	Summary of Drug-Related Fatal Adverse Events by System Organ Class and Preferred Term	• MEA116841 • 201607For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative. • MEA116841 + 201607	IA , SAC
3.18.	Safety	AE3	Summary of Non-Serious Drug-Related Adverse Events by Overall Frequency	Required for Plain Language Summary • MEA116841 • 201607For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative. • MEA116841 + 201607	IA , SAC
3.19.	Safety	AE3	Summary of Serious Drug-Related Adverse Events by Overall Frequency	Required for Plain Language Summary • MEA116841 • 201607For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative. • MEA116841 + 201607	IA , SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.20.	Safety	mid_mepo_egpa_lap /interim1 Table 3.16	Summary of All Cardiovascular Events Reported by the Investigator	• MEA116841 • 201607For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative. • MEA116841 + 201607	IA , SAC
Adverse Events of Special Interest					
3.21.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.17	Summary of On-Treatment Adverse Events of Special Interest: Systemic Reactions	• MEA116841 • 201607	IA , SAC
3.22.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.18	Summary of On-Treatment Adverse Events of Special Interest: Systemic Reactions, by Whether Related to Investigational Product	• MEA116841 • 201607	IA , SAC
3.23.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.19	Summary of Systemic Reactions Experienced on Day of Dosing	• MEA116841 • 201607	IA , SAC
3.24.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.20	Summary of On-Treatment Adverse Events of Special Interest: Systemic Hypersensitivity Reactions	• MEA116841 • 201607	IA , SAC
3.25.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.21	Summary of On-Treatment Adverse Events of Special Interest: Systemic Non-Allergic Reactions	• MEA116841 • 201607	IA , SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.26.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.22	Summary of On-Treatment Adverse Events of Special Interest: Local Injection Site Reactions	• MEA116841 • 201607	IA , SAC
3.27.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.23	Summary of On-Treatment Adverse Events of Special Interest: Local Injection Site Reactions, by Whether Related to Investigational Product	• MEA116841 • 201607	IA , SAC
3.28.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.24	Summary of On-Treatment Adverse Events of Special Interest: Systemic Reactions That According to Investigator Met Criteria for Anaphylaxis	• MEA116841 • 201607	IA , SAC
3.29.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.25	Summary of On-Treatment Adverse Events of Special Interest: Potential Opportunistic Infections	• MEA116841 • 201607	IA , SAC
3.30.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.26	Summary of On-Treatment Adverse Events of Special Interest: Malignancies	• MEA116841 • 201607	IA , SAC
3.31.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.27	Summary of On-Treatment Adverse Events of Special Interest: Serious Cardiac, Vascular and Thromboembolic	• MEA116841 • 201607	IA , SAC
3.32.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.28	Summary of On-Treatment Adverse Events of Special Interest by Cardiovascular History or Risk: Serious Cardiac, Vascular and Thromboembolic	• MEA116841 • 201607	IA , SAC
3.33.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.29	Summary of On-Treatment Adverse Events of Special Interest: Serious Ischemic Events	• MEA116841 • 201607	IA , SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.34.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.30	Summary Profile of On-Treatment Adverse Events of Special Interest: Systemic Reactions	• MEA116841 • 201607	IA , SAC
3.35.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.31	Summary Profile of On-Treatment Adverse Events of Special Interest: Systemic Hypersensitivity Reactions	• MEA116841 • 201607	IA , SAC
3.36.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.32	Summary Profile of On-Treatment Adverse Events of Special Interest: Systemic Non-Allergic Reactions	• MEA116841 • 201607	IA , SAC
3.37.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.33	Summary Profile of On-Treatment Adverse Events of Special Interest: Local Injection Site Reactions	• MEA116841 • 201607	IA , SAC
3.38.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.34	Summary Profile of On-Treatment Adverse Events of Special Interest: Potential Opportunistic Infections	• MEA116841 • 201607	IA , SAC
3.39.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.35	Summary Profile of On-Treatment Adverse Events of Special Interest: Malignancies	• MEA116841 • 201607	IA , SAC
3.40.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.36	Summary Profile of On-Treatment Adverse Events of Special Interest: Serious Cardiac, Vascular and Thromboembolic	• MEA116841 • 201607	IA , SAC
3.41.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.37	Summary Profile of On-Treatment Adverse Events of Special Interest: Serious Ischemic Events	• MEA116841 • 201607	IA , SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure-Adjusted Adverse Events					
3.42.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.38	Summary of Exposure Adjusted On-Treatment Adverse Events	• MEA116841 • 201607	IA , SAC
3.43.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.39	Summary of Exposure Adjusted Most Frequent On-Treatment Adverse Events Reported by 3% or More Subjects In Any Treatment Group	• MEA116841 • 201607	IA , SAC
3.44.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.40	Summary of Exposure Adjusted Drug Related Adverse Events	• MEA116841 • 201607	IA , SAC
3.45.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.41	Summary of Exposure Adjusted On-Treatment Adverse Events Leading To Permanent Discontinuation of Study Drug or Withdrawal From Study	• MEA116841 • 201607	IA , SAC
3.46.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.42	Summary of Exposure Adjusted On-Treatment Serious Adverse Events	• MEA116841 • 201607	IA , SAC
3.47.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.43	Summary of On-Treatment Adverse Events by Age Category	• MEA116841 • 201607	IA , SAC
3.48.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.44	Summary of On-Treatment Adverse Events by Sex	• MEA116841 • 201607	IA , SAC
3.49.	Safety	*mid_mepo_egpa_lap /interim1* Table 3.45	Summary of On-Treatment Adverse Events by Race	• MEA116841 • 201607201607	IA , SAC

9.7.6. ICH Listings

All listings will include the following study IDs unless otherwise specified:

- MEA116841
- 201607

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	All Subjects Enrolled	ES7	Listing of Reasons for Screen Failure		IA , SAC
2.	All Subjects Enrolled	ES2 / ES3	Listing of Reasons for Study Withdrawal		IA , SAC
3.	Safety	SD2/SD3	Listing of Reasons for Study Treatment Discontinuation		IA , SAC
Protocol Deviations					
4.	Safety	DV2	Listing of Important Protocol Deviations	• MEA116841 only	IA , SAC
5.	Safety	IE3	Listing of Participants with Inclusion/Exclusion Criteria Deviations	• MEA116841 only	IA , SAC
Populations Analysed					
6.	Safety	SP3/SP3a	Listing of Participants Excluded from Any Population	Subjects screened but not included in Safety Population	IA , SAC
Demographic and Baseline Characteristics					
7.	Safety	DM2 / DM4	Listing of Demographic Characteristics		IA , SAC
8.	Safety	DM9 / DM10	Listing of Race		IA , SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure and Treatment Compliance					
9.	Safety	See *mid_mepo_egpa_lap/interim1* Listing 10	Listing of Exposure Data		IA , SAC
10.	Safety	See *mid_mepo_egpa_lap/interim1* Listing 26	Listing of Current and Previous Treatment		IA , SAC
Adverse Events					
11.	Safety	AE8	Listing of All Adverse Events		IA , SAC
12.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events		IA , SAC
13.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text		IA , SAC
Serious and Other Significant Adverse Events					
14.	Safety	AE8	Listing of Fatal Serious Adverse Events		IA , SAC
15.	Safety	AE8	Listing of Non-Fatal Serious Adverse Events		IA , SAC
16.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event		IA , SAC
17.	Safety	AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment		IA , SAC
18.	Safety	See *mid_mepo_egpa_lap/interim1* Listing 19	Listing of Adverse Events Defined by the Investigator as a Systemic (Non-Allergic or Allergic/Hypersensitivity) Injection Reaction		IA , SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
19.	Safety	See *mid_mepo_egpa_lap/interim1* Listing 20	Listing of Adverse Events Defined by the Investigator as a Local Injection Site Reaction		IA , SAC
20.	Safety	See *mid_mepo_egpa_lap/interim1* Listing 21	Listing of AEs of Systemic Reactions Meeting Anaphylaxis Criteria		IA , SAC
21.	Safety	See *mid_mepo_egpa_lap/interim1* Listing 22	Listing of Potential Opportunistic Infections		IA , SAC
22.	Safety	See *mid_mepo_egpa_lap/interim1* Listing 23	Listing of Serious Ischemic AEs		IA , SAC
23.	Safety	See *mid_mepo_egpa_lap/interim1* Listing 24	Listing of Malignancies		IA , SAC
Corticosteroid Medication					
24.	Safety	See *mid_mepo_egpa_lap/interim1* Listing 11	Listing of Corticosteroid Therapy		IA , SAC