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

Title	:	Reporting and Analysis Plan for An open-label, randomized, parallel group, single dose study to investigate the PK and safety of belimumab 200 mg intravenous and 200 mg subcutaneous via auto-injector in Chinese healthy participants
Compound Number	:	GSK1550188
Clinical Study Identifier	:	209629
Effective Date	:	27-Feb-2020

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 209629/Amendment 01.
- This RAP is intended to describe the pharmacokinetics and safety analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.

RAP Author(s):

Author	Date
Lead	07-Jan-2020
PPD Senior Statistician, Statistics & Programming, R&D China	

RAP Team Reviews:

RAP Team Review Confirmations
(Method: E-mail)

Reviewer	Date
PPD Associate Director, CPMS, R&D China	13-Jan-2020
PPD Senior Clinical Research Physician, R&D China	09-Jan-2020
PPD Senior Study Manager, R&D China	07-Jan-2020
PPD Senior Clinical Data Scientist, R&D China	08-Jan-2020
PPD Senior Statistical Analyst I, MacroStat (China) Clinical Research Co., Ltd. (Wuhan)	10-Jan-2020

Clinical Statistics and Clinical Programming Line Approvals:

Clinical Statistics & Clinical Programming Line Approvals
(Method: E-mail)

Approver	Date
PPD Associate Director, Statistics & Programming, R&D China	27-Feb-2020

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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:		
209629	18-Mar-2019	Original
209629/Amendment 01	27-Jun-2019	The changes made aim to increasing operational feasibility and consistency with clinical study practice at the study site. Key changes including: • Time of pre-dose blood sampling changed from point to a time window. • Changing method to collect blood pressure, body temperature; and pulse rate is replaced by heart rate to better reflect clinical practice. • Correction of other inconsistency and typos.

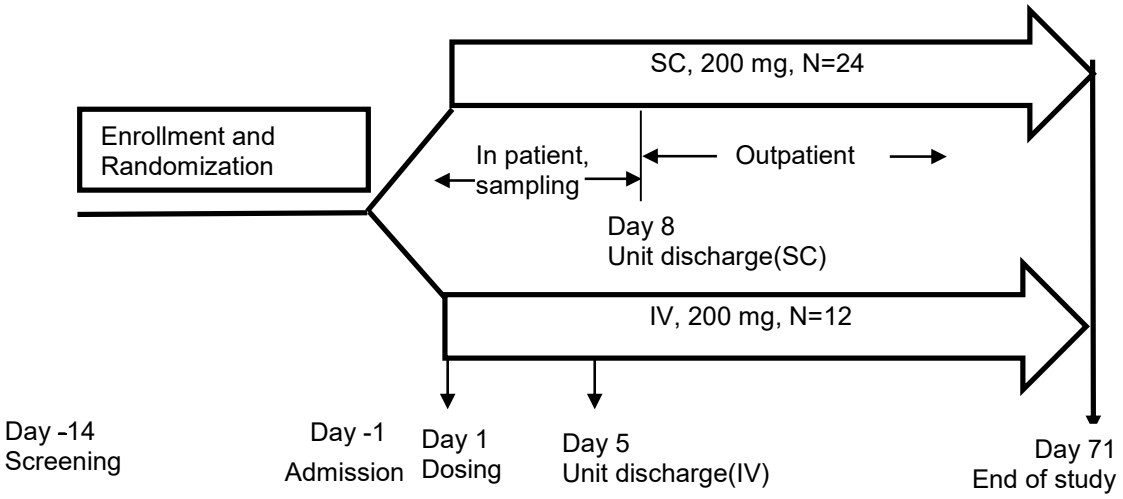
2. SUMMARY OF KEY PROTOCOL INFORMATION

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

Objectives	**Endpoints**
Primary	**Primary**
To characterize the PK profile of belimumab 200 mg after intravenous and subcutaneous administration via auto-injector in healthy Chinese participants	Individual concentration-time profiles, and median/mean profiles of belimumab by treatment groups.
Secondary	**Secondary**
To evaluate the safety and tolerability of IV and SC administration via auto-injector of belimumab 200 mg in healthy Chinese participants	Safety parameters including vital signs, ECGs, clinical laboratory test, local tolerance evaluation (injection site), and adverse events.

2.2. Study Design

Overview of Study Design and Key Features



Design Features	• This is an open-label, randomized, parallel group, single dose study in healthy Chinese participants. Each participant will be randomized at 1:2 ratio to receive one treatment of either IV or SC administration of belimumab 200 mg. The intravenous dose will be administered over approximately 1 hour. The diluted solution volume for IV will be 250 mL in total. The subcutaneous dose will be administered in the front of the thigh via auto-injector device within approximately 15 seconds. The total study duration is approximately 13 weeks.
Dosing	• Subjects will be randomized at 1:2 ratio to receive single dose of either IV or SC administration of belimumab 200 mg.
Time & Events	• Refer to Appendix 2: Schedule of Activities
Treatment Assignment	• Randomization will be stratified by body weight (<65 kg and ≥65 kg). • In each stratum, the participants will be allocated to the two treatment groups by 1: 2 (IV:SC) ratio.
Interim Analysis	• No interim analysis is planned in the study.

2.3. Statistical Hypotheses / Statistical Analyses

The primary objective of this study is to characterize the PK profile of belimumab 200 mg after intravenous and subcutaneous administration in health Chinese participants. There is no formal hypothesis to be tested.

3. PLANNED ANALYSES

3.1. Interim Analyses

No interim analysis is planned in the study.

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), source data lock (SDL) and database freeze (DBF) have been declared by Data Management.
3. Randomization codes have been distributed according to RandAll NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Enrolled	• All participants who sign the ICF	• Screen Failures • Populations for Analyses
Safety	• All randomized participants who take at least 1 dose of study treatment. Participants will be analyzed according to the treatment they actually received.	• Study Population • Safety
Pharmacokinetic Population	• The PK Population will include all participants in the Safety population for whom at least one evaluable PK sample will be obtained and analysed.	• PK Analyses

Refer to Appendix 12: List of Data Displays which details the population used for each display.

4.1. Protocol Deviations

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

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan 22Jul2019 V1.0.

- 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 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 Randomization System		Data Displays for Reporting	
Code	Description	Description	Order in TLF
A	Belimumab 200 mg single IV	Belimumab 200 mg IV	1
B	Belimumab 200 mg single SC	Belimumab 200 mg SC	2

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline. The change from baseline will be calculated by subtracting the baseline values from the individual post-baseline values. If either the baseline or post-baseline value is missing, the change from baseline is set to missing as well.

Parameter	Study Assessments Considered as Baseline			Baseline Used in Data Display
	Screening	Day -1	Day 1 (Pre-Dose)	
Safety				
Hematological/Chemical/Urinalysis tests	X	X		Day -1
Immunological tests	X			Screening
Vital Signs	X	X	X	Day 1
12-Lead ECG	X			Screening

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

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
10.3	Appendix 3: Assessment Windows
10.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
10.5	Appendix 5: Data Display Standards & Handling Conventions
10.6	Appendix 6: Derived and Transformed Data
10.7	Appendix 7: Reporting Standards for Missing Data
10.8	Appendix 8: 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 "Safety" population, unless otherwise specified. Screen failures will be listed and summarized based on "Enrolled" population.

Study population analyses including analyses of participant's disposition, protocol deviations, demographic and baseline characteristics, concomitant medications, and exposure will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 12: List of Data Displays.

6.2. Disposition of Subjects

The number and percentage of completers and withdrawal subjects with the reason for withdrawal will be summarized by treatment group.

The subject who prematurely withdrew will be listed with treatment, subject ID, date of withdrawal, study day of withdrawal, and primary reason for withdrawal.

6.3. Protocol Deviations

A listing of the inclusion/exclusion criteria deviation record for all subjects with deviations will be provided.

A summary of important protocol deviations and by-subject listing of important protocol deviations will be provided. The summary will be displayed by treatment group and overall.

6.4. Demographic and Baseline Characteristics

6.4.1. Demographic characteristics

Demographic characteristics listed below will be summarized either with descriptive statistics including the number of subjects, mean, standard deviation, median, minimum, and maximum for continuous variables or with number and percentage for categorical variables. A by-subject listing of these characteristics will be provided.

- Continuous variables: Age, Height, Weight, and Body mass index (BMI)
- Categorical Variables: Sex, Weight (<65 kg and ≥65 kg), Ethnicity and Geographic Ancestry.

The summary will be displayed by treatment group and overall for demographic characteristics. The age on the start date of treatment will be calculated (See Section 10.6.2). The height observed at Screening and body weight and BMI at Day -1 will be used to prepare the summary table and listing of demographics.

6.5. Concomitant Medications

The concomitant medications recorded on eCRF will be listed using generic terms with treatment, subject ID, indication, dose, unites, frequency, route, start date, study day, stop date, flag for started pre-trial and flag for ongoing medication.

6.6. Medical Conditions

The medical conditions recorded on eCRF will be listed with treatment, subject ID, condition and status.

7. SAFETY ANALYSES

The safety analyses will be based on the "Safety" population, unless otherwise specified. Safety data will be presented in tabular format and summarized descriptively according to GSK's Integrated Data Standards Library (IDSL) standards.

7.1. Extent of Exposure

The following data regarding exposure will be listed: treatment, subject ID, start date and time of dose, stop date and time of dose, duration (minute) and actual dose.

7.2. Adverse Events Analyses

Adverse Events will be coded using MedDRA and summarized by System Organ Class (SOC) and Preferred Term (PT). The number and percentage of participants with any adverse events occurring on or after the treatment start date will be summarized by treatment group. The listing of all adverse events will be prepared.

When adverse events leading to discontinuation, serious adverse events, or other significant adverse events are observed, a listing will be prepared separately.

In the summary of AEs, the incidence of AEs will be the number of subjects reporting AEs and not the number of AEs reported. Multiple occurrences of the same AE in one individual will be counted only once when calculating the number and percentage of subjects.

The following AEs will be summarized and listed:

- All AEs after start of dosing will be summarized by treatment group.
- The drug-related AEs after start of dosing will be summarized by treatment group.
- All AEs after start of dosing will be summarized by treatment group and maximum intensity.
- The drug-related AEs after start of dosing will be summarized by treatment group and maximum intensity.
- All Serious AEs after start dosing will be summarized by treatment group.
- All non-serious AEs after start dosing will be summarized by treatment group.
- All AEs leading to study withdrawals will be summarized by treatment group.
- The relationship among SOC, PT and verbatim text will be listed.
- All AEs after start of dosing will be listed.
- All drug-related AEs after start of dosing will be listed.

- All Serious AEs after start dosing will be listed.
- All non-serious AEs after start of dosing will be listed.
- All AEs leading to study withdrawals will be listed.

The details of the planned displays are provided in Appendix 12: List of Data Displays.

7.3. Adverse Events of Special Interest Analyses

7.3.1. Local tolerance evaluation

The adverse events related to injection site reactions (e.g., induration, erythema, edema, rash, pruritis, pain) will be summarized and identified on the listing for SC group only.

7.4. Clinical Laboratory Analyses

The clinical laboratory values will be summarized by treatment group at each planned time and all observed values will be listed. The change from baseline of each clinical laboratory test will be summarized by treatment group at each planned time. The shift table of the number of subjects with values outside normal ranges will be prepared by treatment group.

The following data will be summarized and listed:

- The clinical laboratory values will be summarized by treatment group at each planned time (Screening, Day -1, Day 8, Day 29, Day 57 and Day 71 for Hematological/Chemical/Urinalysis tests, and Screening, Day 15, Day 29, Day 57 and Day 71 for Immunological tests).
- The change from baseline of each clinical laboratory test will be summarized by treatment group at each planned time (Day 8, Day 29, Day 57, Day 71 for Hematological/Chemical/Urinalysis tests, and Day 15, Day 29, Day 57 and Day 71 for Immunological tests). The baseline is defined as the value observed at Day -1 for Hematological/Chemical/Urinalysis tests and the value observed at Screening for Immunological tests (See Section 5.2).
- The shift table of the number of subjects with values outside normal ranges will be prepared by treatment. The table will be provided for baseline*(Day 8, Day 29, Day 57, Day 71) for Hematological/Chemical/Urinalysis tests and baseline*(Day 15, Day 29, Day 57 and Day 71) for Immunological tests.
- All clinical laboratory data will be listed.

The details of the planned displays are in Appendix 12: List of Data Displays.

7.5. Other Safety Analyses

The analyses of non-laboratory safety test results including vital signs, 12-lead ECGs, and liver events will be based on GSK Core Data Standards, unless otherwise specified.

The details of the planned displays are presented in Appendix 12: List of Data Displays.

7.5.1. Vital signs

The values of vital signs (systolic and diastolic blood pressure, heart rate, tympanic temperature and body weight) will be summarized by treatment group at each planned time (Screening, Day -1, Day 1 Pre-dose, 1h, 2h, 4h, 6h, Day 2 24h, 36h, Day 3 48h, 60h, Day 4 72 h, 84h, Day 5, 6, 7, 8, 11, 15, 22, 29, 43, 57, 71; for body weight, screening, Day -1).

The change from baseline in vital signs will be summarized by treatment group at each planned time (Day 1 1h, 2h, 4h, 6h, Day 2 24h, 36h, Day 3 48h, 60h, Day 4 72 h, 84h, Day 5, 6, 7, 8, 11, 15, 22, 29, 43, 57, 71; The change from baseline for body weight will not be summarized since body weight will not be captured post baseline). For vital signs except for body weight, the observed value at Day 1 pre-dose will be used as the baseline value (See Section 5.2).

All vital signs will be listed at each planned time including the observation at unscheduled visits.

7.5.2. Electrocardiogram

The findings of 12-lead ECG will be summarized by treatment at each planned time (Screening, Day 71).

The values of ECG parameters (heart rate, PR, QRS, QT, and QTc intervals) will be summarized by treatment at each planned time (Screening, Day 71).

The changes from baseline of above parameters will be summarized by treatment group at each planned time (Day 71). The observed value at Screening will be used as the baseline value (See Section 5.2).

Only abnormal ECG findings will be listed.

All values of ECG parameters will be listed including the observation at unscheduled visits.

7.5.3. Liver events

When a liver events has occurred in this study, the appropriate listings will be prepared for the “Safety” population depending on the data collected for the event.

- Listing of liver monitoring/stopping event reporting.
- Listing of liver biopsy details.

- Listing of liver imaging details.
- Listing of liver disease medical conditions

8. PHARMACOKINETIC ANALYSES

8.1. Primary Pharmacokinetic Analyses

8.1.1. Endpoint / Variables

8.1.1.1. Drug Concentration Measures

Briefly, PK samples from approximately 24 subjects in belimumab SC group will be collected at Day 1 pre-dose, 6 h, Day 2 24 h, Day 3 48 h, Day 4 72 h, Day 5 96 h, Day 6 120 h, Day 7 144 h, Day 8 168 h, Day 11 240 h, Day 15 336 h, Day 22 504 h, Day 29 672 h, Day 43 1008 h, Day 57 1344 h, and Day 71 1680 h. In belimumab IV group, PK samples from approximately 12 subjects will be collected at Day 1 pre-dose, -30 mins (after the start of belimumab IV infusion), 0 h (end of infusion), 1 h, 6 h, Day 2 24 h, Day 3 48 h, Day 4 72 h, Day 5 96 h, Day 8 168 h, Day 15 336 h, Day 22 504 h, Day 29 672 h, Day 43 1008 h, Day 57 1344 h, and Day 71 1680 h.

8.1.1.2. Derived Pharmacokinetic Parameters

NA.

8.1.2. Summary Measure

Serum concentrations of belimumab will be listed and summary statistics, including mean, median, standard deviations per GSK IDSL standard, will be calculated by treatment group and nominal time. Individual concentration-time profiles and median/mean profiles by treatment group will be plotted on both a linear and semilog scale.

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Standards for Pharmacokinetic)

8.1.3. Population of Interest

The primary pharmacokinetic analyses will be based on the “Pharmacokinetic” population, unless otherwise specified.

9. REFERENCES

GlaxoSmithKline Document Numbers 2018N385241_01 (Amendment 01, 27-Jun-2019): An open-label, randomized, parallel group, single dose study to investigate the PK and safety of belimumab 200 mg intravenous and 200 mg subcutaneous via auto-injector in Chinese healthy participants.

10. APPENDICES

10.1. Appendix 1: Exclusions from Per Protocol Population

NA.

10.2. Appendix 2: Schedule of Activities

10.2.1. Protocol Defined Schedule of Events

Study Day	Screening (-14~-1)	-1	1									2		3		4	
Hour (Relative to dose completion)			Pre-dose	-1 h	-30 min	0 h	1 h	2 h	4 h	6 h	12 h	24 h	36 h	48 h	60 h	72 h	84h
Informed consent	X																
Outpatient visit	X																
Admission to unit		X															
Demographics and Medical history[a]	X																
Body weight and BMI[b]	X	X															
Height	X																
Inclusion/Exclusion Criteria	X	X	X														
Randomization		X															
Laboratory and Clinical																	
Urine Drug Screen	X																
Alcohol Breath Test		X															
HIV, syphilis, HepB and HepC Screen	X																
Chest X-Ray	X																
QuantiFERON-TB Gold Test	X																
Pregnancy test (female with fertility) [c]	X	X[c]															
12-lead ECG [d]	X																
Hematological/Chemical/Urinalysis tests	X	X[o]															
IgA, IgM and IgG	X																
Physical examination	X	X	X[e]									X[e]		X[e]		X[e]	
Vital signs [f]	X	X	X				X	X	X	X		X	X	X	X	X	X
AE, SAE assessment [g]	←==========																→
Concomitant drug review	←==========																→
Dosing and PK Sampling																	
Study Treatment Dosing IV only				◄—1 h[h]—►													
Study Treatment Dosing SC						X											
PK blood sample IV			X		X[n]	X	X			X		X		X		X	
PK blood sample SC			X							X		X		X		X	
Local tolerance evaluation (SC only) [j]						X[k]	X		X			X[l]		X[l]		X[l]	

Study Day	5	6	7	8	11[i,m]	15[i,m]	22[i,m]	29[i,m]	43[i,m]	57[i,m]	71/Follow-up[i,m]
Hour (Relative to dose completion)	96 h	120 h	144 h	168 h	240 h	336 h	504 h	672 h	1008 h	1344 h	1680 h
Outpatient visit				X[m]	X[i]	X	X	X	X	X	X
Discharge	X[m]			X[i]							
Laboratory and Clinical											
Pregnancy test (Only for female with fertility) [c]								X		X	X
12-lead ECG[d]											X
Hematological/Chemical/Urinalysis tests				X				X		X	X
IgA, IgM and IgG						X		X		X	X
AE, SAE assessment [g]	←==========										→
Concomitant drug review	←==========										→
Physical examination	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X
Vital signs	X	X[i]	X[i]	X	X[i]	X	X	X	X	X	X
PK blood sample IV	X			X		X	X	X	X	X	X
PK blood sample SC	X	X	X	X	X	X	X	X	X	X	X
Local tolerance evaluation (SC only) [j]	X[l]										

a. Medical history includes allergy history, alcohol and smoking history, use of concomitant medication, blood donation history, other clinical trials attendance history, general condition and other which would be assessed as related to the Inclusion/Exclusion Criteria listed in Section 5.1 and Section 5.2.
b. Body weight on day-1 would be used for study stratification.
c. Pregnancy (serum or urine) test is only for female participants with fertility. Urine pregnancy test is required at screening visit, Day 29, Day 57 and Day 71. Serum pregnancy test is required at Day -1. Only conduct serum pregnancy test for subjects screened on Day -1. Pregnancy beyond Day 71 and within 16 weeks will be assessed with a home kit and participants can report the results via phone to site.
d. Single ECG, or triplicate ECGs obtained over a brief recording period.
e. Symptom-driven physical examination.
f. Vital signs include BP (sitting position), heart rate and tympanic temperature. Standing and supine BP will be additionally collected on Day -1.
g. SAE collection will start from inform consent, AE collection will start from study treatment administration. Injection site reactions (e.g., induration, erythema, edema, rash, pruritis, pain) are to be recorded on the AE form of CRF.
h. The IV infusion time will be over and close to 1hour. It's important to record the actual infusion start time and completion time in the medical notes.
i. SC only. The outpatient visits planned for SC is on Day 11,15, 22, 29, 43, 57,71.
j. Local tolerance evaluation: inspection of injection site reactions (e.g., induration, erythema, edema, rash, pruritis, pain) are to be recorded on the AE form of CRF.
k. Immediately after injection completed.
l. Local tolerance evaluation windows on Day 2,3,4,5 are ±4hrs.
m. IV only. The outpatient visits planned for IV is on Day 8,15,22,29,43,57,71.
n. The -30 min PK timepoint is calculated at 30 mins after the start of belimumab IV infusion.

10.3. Appendix 3: Assessment Windows

- Clinic visits are scheduled to take place as specified in Appendix 2: Schedule of Activities. Individual measurements will be reported based on the visits they are assigned to in the study database without adjustment.
- If a circumstance should arise where multiple measurements have been collected and recorded against the same time point, then the first valid value will be used for that time point.

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

10.4.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to the start and/or stop date of the study treatment.

10.4.1.1. Study Phases for Concomitant Medication

No definition of study phases for concomitant medications in this study.

10.4.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Onset time since start time of dosing	AE Onset Date – Dosing Start Date + 1
Duration (Days)	AE Resolution Date – AE Onset Date+1

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.

10.5. Appendix 5: Data Display Standards & Handling Conventions

10.5.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: US
HARP Compound	: GSK1550188
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1].	
Generation of RTF Files	
• Rich Text Format (RTF) and PDF files will be generated for the final reporting effort for use in writing the CSR.	

10.5.2. Reporting Standards

General

• The current GSK Statistical Display Standards in the GSK Standards Library (IDSL) will be applied for reporting, unless otherwise stated (Library 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 Statistical Display 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 GSK Standard Statistical Display 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 GSK Standard Statistical Display Principle 5.05.1).
  • Unscheduled or unplanned readings will be presented within the participant'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 GSK Standard Statistical Display Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to GSK Standard Statistical Display Principals 7.01 to 7.13.	

10.5.3. Reporting Standards for Pharmacokinetic

Pharmacokinetic Concentration Data	
PC Windows Non-Linear (WNL) File	No PK parameter will be provided by this study.
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to the GSK Standard PK Display Standard. Refer to the GSK Standard Statistical Display Principle 6.06.1. Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.
NONMEM/Pop PK File	Not applicable.
NONMEM/PK/PD File	Not applicable.

10.6. Appendix 6: Derived and Transformed Data

10.6.1. General

Multiple Measurements at One Analysis Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • If there are two values within a time window, the value closest to the target day for that window will be used. If values are the same distance from the target, then the mean will be taken.
Study Day

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

10.6.2. Study Population

Age
• Age will be calculated based on the Start date of dose. • Only year of birth is collected on the eCRF, therefore day and month of birth are imputed as '30JUN' in order to derive age. • Birth date will be presented in listings as 'YYYY'.

Body Mass Index (BMI)
• Calculated as **Weight (kg) / [Height (m)]^2**

10.6.3. Safety

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. • Example 1: 2 Significant Digits = '< x ' becomes x – 0.01 • Example 2: 1 Significant Digit = '> x' becomes x + 0.1 • Example 3: 0 Significant Digits = '< x' becomes x – 1

10.6.4. Pharmacokinetic

PK concentration
Descriptive statistics (N, mean, SD, median, minimum, and maximum) will be used to summarize the concentration values of belimumab in plasma at each sampling time point by treatment group. Individual subject concentration data will be listed. Individual plasma concentration-time profiles and median/mean profiles will be plotted. Each of the figures will contain one plot on the untransformed scale (i.e. a linear plot) and one plot on the log transformed scale (i.e. log-linear plot). The concentration data described above will be summarised, listed and plotted based on Pharmacokinetic Concentration Population defined in Section 4

10.7. Appendix 7: Reporting Standards for Missing Data

10.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion as specified in the protocol was defined as completion of all phases of the study including the follow-up visit. • Withdrawn participants were not replaced in the study. • All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

10.7.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: ○ These data will be indicated by the use of a "blank" in participant listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. ○ 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.
PK	• All missing concentrations will be indicated by the use of a "blank" in participant listing displays. No imputation will be taken.

10.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays.
Adverse Events	• The eCRF does not allow for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.
Concomitant Medications/ Medical History	• Partial dates for any concomitant medications recorded in the CRF will not be imputed. • The recorded partial date will be displayed in listings.

10.8. Appendix 8: Values of Potential Clinical Importance

NA.

10.9. Appendix 9: Population Pharmacokinetic (PopPK) Analyses

10.9.1. Population Pharmacokinetic (PopPK) Dataset Specification

NA.

10.9.2. Population Pharmacokinetic (PopPK) Methodology

NA.

10.10. Appendix 10: Pharmacokinetic / Pharmacodynamic Analyses

10.10.1. Pharmacokinetic / Pharmacodynamic Dataset Specification

NA.

10.10.2. Pharmacokinetic / Pharmacodynamic Methodology

NA.

10.11. Appendix 11: Abbreviations & Trade Marks

10.11.1. Abbreviations

Abbreviation	Description
ADaMIG	Analysis Data Model Implementation Guide
AE	Adverse Event
BMI	Body mass index
CDISC	The Clinical Data Interchange Standards Consortium
CRF	Case Report Form
DBF	Database freeze
DBR	Database release
DP	Decimal place
ECG	Electrocardiogram
GSK	GlaxoSmithKline
ICF	Informed Consent Form
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IDSL	Integrated Data Standards Library
IV	Intravenous
Kg	Kilogram
msec	Milliseconds
PC	Pharmacokinetic concentration
PD	Pharmacodynamic
PDF	Portable Document Format
PK	Pharmacokinetic
POPPK	Population Pharmacokinetics
PT	Preferred term
RAP	Reporting and Analysis Plan
RTF	Rich Text Format
SAC	Statistical Analysis Complete
SC	Subcutaneous
SD	Standard deviation
SDL	Source data lock
SDTMIG	Study Data Tabulation Model Implementation Guide
SOC	System organ class
TLF	Tables, listings and figures
WNL	Windows Non-Linear

10.11.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
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10.12. Appendix 12: List of Data Displays

10.12.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.01 to 1.05	
Safety	2.01 to 2.27	
Pharmacokinetic	3.01	3.01 to 3.03
Section	**Listings**	
ICH Listings	1 to 16	
Other Listings	17 to 30	

10.12.2. Mock Example Shell Referencing

Nonstandard specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 13: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population		POP_Tn	POP_Ln
Safety		SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln

NOTES:

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

10.12.3. Deliverables

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

NOTES:

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

10.12.4. Study Population Tables

Study Population Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.01	Safety	ES1	Summary of Subject Disposition		SAC [1]
1.02	Enrolled	ES6	Summary of Screening Status and Reasons for Screen Failures		SAC [1]
Protocol Deviation					
1.03	Safety	DV1	Summary of Important Protocol Deviations		SAC [1]
Population Analysed					
1.04	Enrolled	SP1	Summary of Study Populations		SAC [1]
Demographic and Baseline Characteristics					
1.05	Safety	DM1	Summary of Demographic Characteristics		SAC [1]

10.12.5. Safety Tables

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
2.01	Safety	AE13	Adverse Event Overview		SAC [1]
2.02	Safety	AE1	Summary of All Adverse Events by System Organ Class and Preferred Term		SAC [1]
2.03	Safety	AE1	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term		SAC [1]
2.04	Safety	AE5A	Summary of Adverse Events by System Organ Class and Preferred Term and Maximum Intensity		SAC [1]
2.05	Safety	AE5A	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term and Maximum Intensity		SAC [1]
2.06	Safety	AE1	Summary of Non-serious Adverse Events by System Organ Class and Preferred Term		SAC [1]
Serious and Other Significant Adverse Events					
2.07	Safety	AE1	Summary of Serious Adverse Events by System Organ Class and Preferred Term		SAC [1]
2.08	Safety	AE1	Summary of Adverse Events Leading to Withdrawal from Study by System Organ Class and Preferred		SAC [1]
Adverse Events of Special Interest					
2.09	Safety	AE1	Summary of Adverse Events related to Injection Site Reactions		SAC [1]

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Chemistry					
2.10	Safety	LB1	Summary of Chemistry Laboratory Values		SAC [1]
2.11	Safety	LB1	Summary of Chemistry Changes from Baseline		SAC [1]
2.12	Safety	LB4	Summary of Chemistry Shifts from Baseline Relative to Normal Range		SAC [1]
Laboratory: Hematology					
2.13	Safety	LB1	Summary of Hematology Laboratory Values		SAC [1]
2.14	Safety	LB1	Summary of Hematology Changes from Baseline		SAC [1]
2.15	Safety	LB4	Summary of Hematology Shifts from Baseline Relative to Normal Range		SAC [1]
Laboratory: Urinalysis					
2.16	Safety	LB1	Summary of Urinalysis (Specific Gravity and pH)		SAC [1]
2.17	Safety	LB1	Summary of Urinalysis (Specific Gravity and Ph) Changes from Baseline		SAC [1]
2.18	Safety	LB4	Summary of Urinalysis (Specific Gravity and pH) Shifts from Baseline Relative to Normal Range		SAC [1]
2.19	Safety	UR1	Summary of Urinalysis Dipstick Results		SAC [1]
Laboratory: Immunology					
2.20	Safety	LB1	Summary of Immunology Laboratory Values		SAC [1]
2.21	Safety	LB1	Summary of Immunology Changes from Baseline		SAC [1]

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.22	Safety	LB4	Summary of Immunology Shifts from Baseline Relative to Normal Range		SAC [1]
ECG					
2.23	Safety	EG1	Summary of ECG Findings		SAC [1]
2.24	Safety	EG2	Summary of ECG Values		SAC [1]
2.25	Safety	EG2	Summary of Change from Baseline in ECG Values		SAC [1]
Vital Signs					
2.26	Safety	VS1	Summary of Vital Signs		SAC [1]
2.27	Safety	VS1	Summary of Change from Baseline in Vital Signs		SAC [1]

10.12.6. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetic Concentration					
3.01	PK	PKCT1	Summary of Belimumab Pharmacokinetic Concentration-Time Data		SAC [1]
3.02	PK	PKCT1	Summary of Belimumab Pharmacokinetic Concentration-Time Data in Subjects With Weight <65 kg		SAC [1]
3.03	PK	PKCT1	Summary of Belimumab Pharmacokinetic Concentration-Time Data in Subjects With Weight ≥65 kg		SAC [1]

10.12.7. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetic Concentration					
3.01	PK	PKCF1P	Individual Belimumab Concentration-Time Plot (Linear and Semi-Log)		SAC [1]
3.02	PK	PKCF4	Mean(+SD) Belimumab Concentration-Time Plot (Linear and Semi-Log)		SAC [1]
3.03	PK	PKCF4	Mean(+SD) Belimumab Concentration-Time Plot (Linear and Semi-Log) by weight (<65 kg vs. ≥65 kg)		SAC [1]
3.04	PK	PKCF5	Median(Range) Belimumab Concentration-Time Plot (Linear and Semi-Log)		SAC [1]
3.05	PK	PKCF5	Median(Range) Belimumab Concentration-Time Plot (Linear and Semi-Log) by weight (<65 kg vs. ≥65 kg)		SAC [1]

10.12.8. ICH Listings

ICH: Listings					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Safety	ES2	Listing of Reasons for Study Withdrawal		SAC [1]
Protocol Deviations					
2.	Safety	DV2	Listing of Important Protocol Deviations		SAC [1]
3.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC [1]
Demographic and Baseline Characteristics					
4.	Safety	DM2	Listing of Demographic Characteristics		SAC [1]
5.	Safety	DM9	Listing of Race		SAC [1]
Exposure and Treatment Compliance					
6.	Safety	EX3	Listing of Exposure Data		SAC [1]
Adverse Events					
7.	Safety	AE8	Listing of All Adverse Events		SAC [1]
8.	Safety	AE8	Listing of Drug-related Adverse Events		SAC [1]
9.	Safety	AE8	Listing of Non-serious Adverse Events		SAC [1]

ICH: Listings					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
10.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events		SAC [1]
Serious and Other Significant Adverse Events					
11.	Safety	AE8CPA	Listing of Serious Adverse Events		SAC [1]
12.	Safety	AE8	Listing of Adverse Events Leading to Withdrawal from Study		SAC [1]
All Laboratory					
13.	Safety	LB5	Listing of Laboratory Values: Chemistry		SAC [1]
14.	Safety	LB5	Listing of Laboratory Values: Hematology		SAC [1]
15.	Safety	LB5	Listing of Laboratory Values: Immunology		SAC [1]
16.	Safety	UR2	Listing of Urinalysis Data		SAC [1]

10.12.9. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
17.	Screened	ES7	Listing of Reasons for Screen Failure		SAC [1]
18.	Safety	TA1	Listing of Planned and Actual Treatments		SAC [1]
Prior and Concomitant Medications					
19.	Safety	CM3	Listing of Concomitant Medications		SAC [1]
20.	Safety	MH2	Listing of Medical Conditions		SAC [1]
Adverse Events					
21.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text		SAC [1]
22.	Safety	AE8	Listing of Adverse Events related to Injection Site Reactions		SAC [1]
Liver Events					
23.	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting		SAC [1]
24.	Safety	LIVER7	Listing of Liver Biopsy Details		SAC [1]
25.	Safety	LIVER8	Listing of Liver Imaging Details		SAC [1]

Non-ICH: Listings					
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
26.	Safety	N/A	Listing of Liver Disease Medical Conditions		SAC [1]
ECG					
27.	Safety	EG3	Listing of ECG Values for All Subjects		SAC [1]
28.	Safety	EG5	Listing of Abnormal ECG Findings		SAC [1]
Vital Signs					
29.	Safety	VS4	Listing of Vital Signs for All Subjects		SAC [1]
PK Endpoints					
30.	PK	PK07	Listing of Pharmacokinetic Concentration-Time Data		SAC [1]

10.13. Appendix 13: Example Mock Shells for Data Displays

The data display shells are contained in separate documents which are available on request.