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

Title	:	Reporting and Analysis Plan for study 208564: A phase 1, randomised, double-blind, placebo-controlled study of the safety, tolerability, pharmacokinetics and pharmacodynamics of single subcutaneous doses of GSK2330811 in healthy Japanese participants.
Compound Number	:	GSK2330811
Effective Date	:	Refer to Document Date

Description:

- The purpose of the final RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 208564.
- This RAP will be provided to the study team members to convey the Statistical Analysis Complete (SAC) deliverables.

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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 208564:

Revision Chronology:		
2019N406151_00	11-SEP-2019	Original

2. SUMMARY OF KEY PROTOCOL INFORMATION

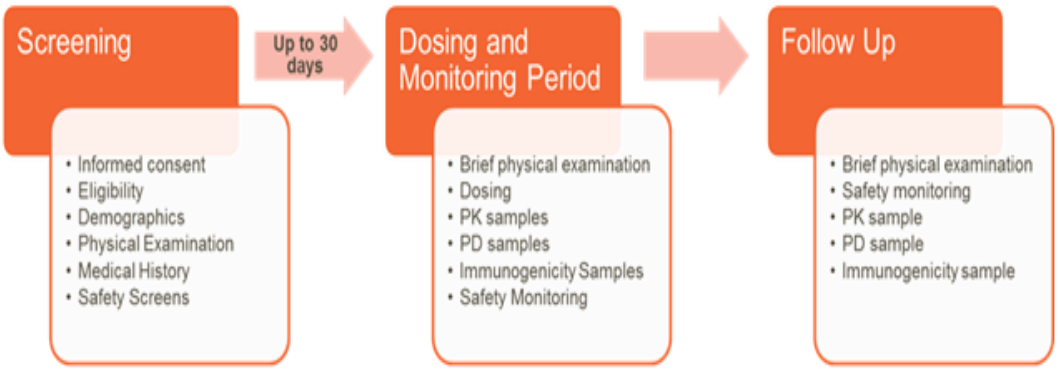
2.1. Changes to the Protocol Defined Statistical Analysis Plan

There was an unplanned interim analysis conducted due to safety related temporary study hold criterion being met and was not specified in the protocol.

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

Objectives	**Endpoints**
Primary Objectives	**Primary Endpoints**
• To evaluate the safety and tolerability of a single SC dose of GSK2330811 in healthy Japanese participants	• Number of participants reporting AEs. • Number of participants reporting SAEs. • Number of participants with vital signs (blood pressure, heart rate, body temperature) reaching a threshold of potential clinical importance • Number of participants with treatment emergent abnormal ECG findings. • Number of participants with CTCAE grade 1 or higher safety laboratory results (clinical chemistry, haematology values where CTCAE grading applies). • Number of participants with treatment emergent abnormal urinalysis findings
Secondary Objectives	**Secondary Endpoints**
• To evaluate the pharmacokinetic (PK) profile of a single SC dose of GSK2330811 in healthy Japanese participants	• Pharmacokinetic parameters (Cmax, AUC, CL/F, Tmax, $t_{1/2}$, Vss/F)
• To assess the potential for anti-drug antibody formation following a single SC dose of GSK2330811 in healthy Japanese participants	• Number of participants with anti-GSK2330811 antibodies
• To assess effects of GSK2330811 on platelets and haemoglobin in healthy Japanese participants	• Platelet nadir • Time to platelet nadir • Haemoglobin nadir • Time to haemoglobin nadir
Exploratory Objectives	**Exploratory Endpoints**
• To explore the PD and the PK/PD relationship for GSK2330811 in the blood of healthy Japanese participants	• Serum levels of free OSM • Serum levels of total OSM • Levels of Thrombopoietin (TPO) • Levels of Erythropoietin (EPO)

2.3. Study Design

Overview of Study Design and Key Features	
	
Design Features	This is a randomised, double-blind, placebo-controlled, single-centre study with single SC doses of GSK2330811 administered to healthy male Japanese participants. • Participants will attend a screening visit at the clinical unit within 30 days of Study Day 1. If eligible for the study, participants will return on Day -1 for overnight admission to the unit. • Participants will be randomized to either GSK2330811 or placebo in an approximate ratio of 7:3. • Approximately 10 eligible participants will be admitted to the clinical unit on the day prior to dosing (Day-1). On Day 1, each participant will receive a single SC dose of GSK2330811 or placebo, administered as three separate SC injections Participants will then remain as an in-patient until discharged on Day 2 after assessments have been performed. • Participants will then return to the clinical unit for outpatient visits as described in the Schedule of Activities (SoA). • The final follow up visit will be at the clinical unit on Day 126. • The maximum dose will not exceed 450mg SC.
Dosing	• Participants will be dosed once on Day 1
Time & Events	• Refer to Appendix 1: Schedule of Activities
Treatment Assignment	• Participants will be assigned to either 450mg GSK2330811 SC or placebo in a 7:3 ratio.
Interim Analysis	• No interim analyses will be performed

2.4. Statistical Analyses

The primary objective of this study is to determine the safety and tolerability of single subcutaneous doses of GSK2330811 in healthy Japanese participants. No formal hypotheses are being tested in this study and therefore no statistical analysis is planned.

2.5. Interim Analyses

An unplanned unblinded review of available exposure time-course data from the ongoing study cohort was initiated due to a safety related temporary study hold criterion being met. The unblinded data provided to CPMS and analysis report was documented in trial master file.

2.6. 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.
3. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed according to RandAll NG procedures.

3. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants who signed the ICF and were screened for eligibility	• Study Population • Screen Failures
Enrolled	• All participants who signed the ICF and were randomized into the study.	• Study Population
Safety	• All randomized participants who received a full dose of study treatment. • Participants will be analysed according to the treatment they received. • Note: In the very unlikely case a participant is not randomized but receives at least one dose of study treatment, these participants will be listed separately.	• Study Population • Safety • PK/PD selected tables and figures
Pharmacokinetic (PK)	• All participants in the Safety population who received at least one active dose of study treatment and had at least 1 non-missing PK assessment (Non-quantifiable values will be considered as non-missing values). • Participants will be analysed according to the study treatment they received.	• PK • PK/PD selected figures

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

3.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, participant management or participant 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 **[Version 1, 25 Nov 2019]**.

- Data will be reviewed prior to unblinding and 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.

A separate table and listing of all COVID-19 related protocol deviations will be provided to capture the impact on visits and assessments.

4. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

4.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		**Data Displays for Reporting**	
Code	**Description**	**Description**	**Order in TFL[1]**
A	GSK2330811 450 mg **SC - PARALLEL**	GSK2330811 450 mg	2
P	Placebo - **PARALLEL**	Placebo	1

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.

4.2. Baseline Definitions

For all endpoints 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 (or Day -1 where applicable) assessments are assumed to be taken prior to first dose and used as baseline.

In case that triplicate assessments are performed, the mean of triplicate assessments at any given time point will be used as the value for that time point.

4.2.1. Derivations and Handling of Missing Baseline Data

If baseline data is missing, no derivation will be performed, and baseline will be set to missing. The baseline definition will be footnoted on all change from baseline displays.

Definition	Reporting Details
Change from Baseline	= Post-Dose Visit – Baseline
% Change from Baseline	= 100 x [(Post-Dose Visit – Baseline) / Baseline]
Nadir	= Lowest post-baseline value of endpoint for a participant [1]
Time (Days) to Nadir	= Study Day of Nadir – 1[1]

NOTES:

- 1: When there are multiple instances of the lowest value then the nadir used for reporting will be the earliest occurrence of that value.
- Unless otherwise specified, the baseline definitions specified in Section 4.2. Baseline Definitions will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.
- The baseline definition will be footnoted on all change from baseline displays. 'Note: Baseline is defined as the pre-dose Day 1 assessment, unless unavailable, in which case it is the latest pre-dose assessment.'
- If there are multiple measurements (i.e. ECG) the derivation will be based on the average values where available.

4.3. Examination of Covariates, Other Strata and Subgroups

There is no planned examination of covariates, other strata and subgroup analyses due to the small overall sample size.

4.4. Multiple Comparisons and Multiplicity

There is no adjustment for multiplicity in this phase 1 study.

4.5. 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
12.2	Appendix 2: Assessment Windows
12.3	Appendix 3: Study Phases and Treatment Emergent Adverse Events
12.4	Appendix 4: Data Display Standards & Handling Conventions
12.5	Appendix 5: Derived and Transformed Data
12.6	Appendix 6: Reporting Standards for Missing Data
12.7	Appendix 7: Values of Potential Clinical Importance

5. STUDY POPULATION ANALYSES

5.1. Overview of Planned Study Population Analyses

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

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

6. EFFICACY ANALYSES

There are no efficacy analyses included in this study.

7. SAFETY ANALYSES

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

7.1. Adverse Events Analyses

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

7.2. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of chemistry laboratory tests, haematology laboratory tests, urinalysis, and liver function tests will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 9: List of Data Displays.

Descriptive statistics (n, arithmetic mean, standard deviation, median, minimum, and maximum) will be calculated for nadirs for platelet count and haemoglobin.

Descriptive statistics (n, median, minimum, maximum and range) will also be calculated for time to nadir for platelet count and haemoglobin.

Laboratory safety will be graded using CTCAE criteria version 5. CTCAE grade 1 or higher safety laboratory results will be presented (where CTCAE grading applies).

7.3. Other Safety Analyses

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

A separate listing to capture the COVID-19 infection assessment of participants based on new eCRF page will be provided.

The details of the planned displays are presented in Appendix 9: List of Data Displays.

8. IMMUNOGENICITY ANALYSES

The immunogenicity analyses will be based on the “Safety” population, unless otherwise specified. The immunogenicity analysis summarises the incidence of confirmed anti-drug antibodies and lists the titre of immunogenicity results.

Details of the planned displays are presented in Appendix 9: List of Data Displays.

9. PHARMACOKINETIC ANALYSES

9.1. Secondary Pharmacokinetic Analyses

9.1.1. Endpoint / Variables

9.1.1.1. Drug Concentration Measures

Refer to Appendix 4: Data Display Standards & Handling Conventions (Section 12.4.3 Reporting Standards for Pharmacokinetic).

9.1.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin. All calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters listed will be determined from the plasma concentration-time data, as data permits.

Parameter	Parameter Description
Cmax	• Maximum observed concentration. Determined directly from the concentration-time data.
Tmax	• Time to reach Cmax. Determined directly from the concentration-time data.
AUC(0-t)	• Area under the concentration-time curve from time zero to the time of last quantifiable concentration (C(t)). • Calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC(0-inf)	• Area under the concentration-time curve from time zero to infinity • Calculated as AUC(0-inf)=AUC(0-t)+C(t)/lambda_z. AUC(0-inf) should not be reported if the area coming from extrapolation is greater than 20% of AUC(0-inf).
%AUCex	• The percentage of AUC (0-inf) obtained by extrapolation will be calculated as: [AUC(0-inf) – AUC(0-t)] / AUC(0-inf) x 100
t1/2	• Terminal half-life • Calculated as t1/2=ln2/lambda_z.
CL/F	• Apparent systemic clearance
Vss/F	• Apparent volume of distribution at steady state
tlast	• Time of last quantifiable concentration

NOTES:

- Additional parameters may be included as required.
- lambda_z is the first order rate constant associated with the terminal (log-linear) portion of the curve. Estimated by linear regression of time vs. log concentration

9.1.2. Summary Measure

Descriptive statistics (n, arithmetic mean, standard deviation [SD], 95% CI, minimum, median and maximum) will be calculated for all PK concentrations over time and for the

derived PK parameters. In addition, for log-transformed PK parameter variables (i.e. Cmax, AUC(0-t), AUC(0-inf), CL/F, Vss/F, t1/2), geometric mean, 95% CI and $\%CV_b$ will be provided. Plots of mean concentrations will also include standard deviation [SD] for the mean.

9.1.3. Population of Interest

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

9.1.4. Strategy for Intercurrent (Post-Randomization) Events

A 'While on-study' strategy will be implemented for intercurrent events.

- Withdrawn participants may be replaced in the study. Replacement participants will be dosed with the planned treatment of the withdrawn participant.

- All available data from participants who were withdrawn from the study will be analysed and listed, and all available planned data will be included in summary tables and figures, unless otherwise specified.

- Non quantifiable data will be handled as per GUI_51487

- If anomalous concentration data is identified, the pharmacokineticist will:

    - excludes the PK concentration data deemed to be anomalous

    - documents the reason for exclusion in the 'Code' folder of the Phoenix Project

    - communicates exclusion to Statistics and Programming

Note: Any exclusion of anomalous PK concentration data is documented in the clinical study report (CSR). Anomalous PK data is excluded from PK summaries and is flagged by asterisk or appropriate footnote in the PK data listings.

10. PHARMACODYNAMIC AND / OR BIOMARKER ANALYSES

10.1. Exploratory Pharmacodynamic (and / or Biomarker) Analyses

10.1.1. Endpoint / Variables

Parameter	Parameter description
Free OSM	Free OSM concentration in serum
Total OSM	Total OSM concentration in serum
TPO	Thrombopoietin concentration in serum
EPO	Erythropoietin concentration in platelet-poor plasma

10.1.2. Summary Measure

Descriptive statistics (n, arithmetic mean, standard deviation [SD], 95% CI, minimum, median and maximum) will be calculated for free and total OSM concentrations over time. Descriptive statistics (n. geometric mean and standard deviation [SD] on log scale, CVb%) will be calculated for log transformed total OSM concentration and ratio to baseline. Plots of individual, mean concentrations with SD and median concentrations with range for total OSM will be produced.

Total OSM parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin. All calculations of non-compartmental parameters will be based on actual sampling times. Total OSM, Cmax, Tmax, AUC(0-t), AUC(0-inf), %AUCex, t1/2, CL/V, Vss/V, tlast might be calculated with non-compartmental analysis, from the serum concentration-time data, as data permits.

Only data listing provided for TPO and EPO concentrations.

10.1.3. Population of Interest

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

10.1.4. Strategy for Intercurrent (Post-Randomization) Events

A ‘While on-study’ strategy will be implemented for intercurrent events.
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.

10.1.5. 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 10.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

11. REFERENCES

GSK Document Number 2019N406151_00. Study ID 208564: A phase 1, randomised, double-blind, placebo-controlled study of the safety, tolerability, pharmacokinetics and pharmacodynamics of single subcutaneous doses of GSK2330811 in healthy Japanese participants.11-SEP-2019.

12. APPENDICES

12.1. Appendix 1: Schedule of Activities

12.1.1. Protocol Defined Schedule of Events

Screening Period

Screening Procedure	Screening (up to 30 days prior to Day 1)
Informed Consent	X
Inclusion and Exclusion Criteria	X
Demography	X
Full Physical Exam (incl. weight and height)	X
Medical History and current medical conditions[1]	X
Concomitant Medication Review	X
12 lead ECG in triplicate	X
Vitals (blood pressure, heart rate, body temperature)[2]	X
Breath Alcohol Screen	X
Urine Drug Screen	X
HIV, HBV and HCV Screen	X
Tuberculosis (TB) Screening QuantiFERON	X
Haematology/Clinical Chemistry/Urinalysis/Clotting	X
SAE Review	X

1. To include substance usage, family history of premature cardiovascular disease, medication, drug/alcohol history
2. Vital signs are to be taken before blood collection for laboratory tests.

Treatment and Follow-Up Period

Procedure	Day -1	Day 1					Day 2	Day 3	Day 5	Day 7	Day 10 ±1 day	Day 14 ±1 day	Day 21 ±1 day	Day 28 ±1 day	Day 42 ±2 days	Day 56 ±2 days	Day 84 ±7 days	Day 126 (follow-up visit)/Early Withdrawal ±7 days
Admission	X																	
In-patient Stay	X	X																
Discharge							X											
Outpatient Visit								X	X	X	X	X	X	X	X	X	X	X
Inclusion and Exclusion Criteria	X																	
Breath Alcohol Screen	X																	
Urine Drug Screen	X																	
		Pre-dose	**0h**	**1h**	**4h**	**8h**	**24h**											
Dosing[3]			X															
Injection Site Reaction Assessment		X[5]	X[5]		X[5]		X[5]											X
Brief Physical Exam	X						X[1]											
Full Physical Exam[6]																		X
Haematology/Clinical Chemistry	X	X[2]					X[1]	X	X	X	X	X	X[2]	X	X	X	X	X
Urinalysis	X									X			X				X	X
12 lead ECG (triplicate)		X								X			X				X	X
Vitals (blood pressure, heart rate, body temperature)[4]	X	X		X[1]	X[1]	X[1]	X[1]	X	X	X	X	X	X	X	X	X	X	X
PK Sampling		X				X[1]	X[1]	X	X	X	X	X	X	X	X	X	X	X
Free & Total OSM Sampling		X				X[1]	X[1]	X	X	X	X	X	X	X	X	X	X	X
Immunogenicity Sampling		X										X		X				X
TPO Sampling		X							X		X		X				X	
EPO Sampling		X								X		X	X			X		
Concomitant Medication Review		Monitored from screening until end of follow-up visit																
SAE/AE Review		SAEs collected from signing of consent form, AEs collected continuously from time of dose																

Footnotes:
1. All post dose time points are in reference to the first injection of IMP.
2. Day 1 Pre-dose sample and Day 21 sample will be fasted for approximately 12 hr and will include lipids
3. IMP administration consists of 3 syringes, all 3 syringes are to be administered as closely together in time as possible
4. Vital signs are to be taken before blood collection for laboratory tests.
5. Assessments should be conducted immediately before first injection (pre-dose) and immediately after last injection (0h). Post dose assessments (4h and 24h) to be conducted in reference to the last injection of IMP. Any injection site reactions to be captured through AE reporting.
6. Full physical exam at follow-up will not include height

- The timing and number of planned study assessments may be altered during the course of the study based on newly available data (e.g., to obtain data closer to the time of peak plasma concentrations) to ensure appropriate monitoring.
- Any changes in the timing or addition of time points for any planned study assessments as the result of emerging pharmacokinetic/pharmacodynamic data from this study must be documented and approved by the relevant study team member and then archived in the sponsor and site study files but will not constitute a protocol amendment. The Competent Authority (CA) and ethics committee (EC) will be informed of any safety issues that constitute a substantial amendment and require alteration of the safety monitoring scheme or amendment of the informed consent form (ICF). The changes will be approved by the CA and the EC before implementation.

12.2. Appendix 2: Assessment Windows

For haematology, chemistry, vital signs, ECG, urinalysis, immunogenicity, PK and biomarker outputs (incl. summaries and figures), Unscheduled and early withdrawal assessments will be included (see Appendix 4: Data Display Standards & Handling Conventions and Appendix 9: List of Data Displays).

Where unscheduled and early withdrawal visits are included in outputs, the following visit slotting will apply. If more than one visit slots to the same analysis timepoint, the closest visit to the analysis timepoint will be included in the summary and figure.

12.2.1. Definitions of Assessment Windows for Analyses

Analysis Set / Domain	Analysis Window		Analysis Timepoint
	Beginning Timepoint	Ending Timepoint	
Haematology and Chemistry	Days less than 0		Screening
	Day 1	Day 1	Day 1
	Day 2	Day 2	Day 2
	Day 3	Day 4	Day 3
	Day 5	Day 6	Day 5
	Day 7	Day 8	Day 7
	Day 9	Day 12	Day 10
	Day 13	Day 17	Day 14
	Day 18	Day 24	Day 21
	Day 25	Day 34	Day 28
	Day 35	Day 49	Day 42
	Day 50	Day 63	Day 56
	Day 64	Day 105	Day 84
	Day 106	Day 133	Day 126

Analysis Set / Domain	Analysis Window		Analysis Timepoint
	Beginning Timepoint	Ending Timepoint	
Vital signs	Days less than 0		Screening
	Day 1 - Pre dose		Day 1 - Pre dose
	Day 1 - 1H		Day 1 - 1H
	Day 1 - 4H		Day 1 - 4H
	Day 1 - 8H		Day 1 - 8H
	Day 2	Day 2	Day 2
	Day 3	Day 4	Day 3
	Day 5	Day 6	Day 5
	Day 7	Day 8	Day 7
	Day 9	Day 12	Day 10
	Day 13	Day 17	Day 14

Analysis Set / Domain	Analysis Window		Analysis Timepoint
	Beginning Timepoint	Ending Timepoint	
	Day 18	Day 24	Day 21
	Day 25	Day 34	Day 28
	Day 35	Day 49	Day 42
	Day 50	Day 63	Day 56
	Day 64	Day 105	Day 84
	Day 106	Day 133	Day 126

Analysis Set / Domain	Analysis Window		Analysis Timepoint
	Beginning Timepoint	Ending Timepoint	
ECG and Urinalysis	Days less than 0		Screening
	Day 1	Day 1	Day 1
	Day 2	Day 14	Day 7
	Day 15	Day 42	Day 21
	Day 43	Day 105	Day 84
	Day 106	Day 133	Day 126

Analysis Set / Domain	Analysis Window		Analysis Timepoint
	Beginning Timepoint	Ending Timepoint	
PK/ Free and Total OSM	Day 1 - Pre dose		Day 1 - Pre dose
	Day 1 - 8H		Day 1 - 8H
	Day 2	Day 2	Day 2
	Day 3	Day 4	Day 3
	Day 5	Day 6	Day 5
	Day 7	Day 8	Day 7
	Day 9	Day 12	Day 10
	Day 13	Day 17	Day 14
	Day 18	Day 24	Day 21
	Day 25	Day 34	Day 28
	Day 35	Day 49	Day 42
	Day 50	Day 63	Day 56
	Day 64	Day 105	Day 84
	Day 106	Day 133	Day 126

Analysis Set / Domain		Analysis Window		Analysis Timepoint
		Beginning Timepoint	Ending Timepoint	
Biomarker samples (EPO/ TPO)	EPO	Day 1	Day 1	Day 1
		Day 2	Day 9	Day 7

Analysis Set / Domain		Analysis Window		Analysis Timepoint
		Beginning Timepoint	Ending Timepoint	
		Day 10	Day 17	Day 14
		Day 18	Day 34	Day 21
		Day 35	Day 133	Day 56
	TPO	Day 1	Day 1	Day 1
		Day 2	Day 7	Day 5
		Day 8	Day 17	Day 10
		Day 18	Day 34	Day 21
		Day 35	Day 133	Day 86

Analysis Set / Domain	Analysis Window		Analysis Timepoint
	Beginning Timepoint	Ending Timepoint	
Immunogenicity	Day 1	Day 1	Day 1
	Day 10	Day 21	Day 14
	Day 22	Day 56	Day 28
	Day 56	Day 133	Day 126

For PK and PD planned and unplanned assessments will be summarised and listed. PK NCA will use all available data and will use actual relative time, not planned relative time.

For all endpoints an early withdrawal assessment occurred at the time when a planned assessment for that endpoint would have occurred (± the visit window), the early withdrawal visit will be slotted to that planned assessment and included in summaries. Where the plots use time as the x-axis, the early withdrawal visit will be included regardless of when the data was collected relative to the study window. For log type data (i.e. AEs), all early withdrawal data will be included in summaries. All early withdrawal data will be listed.

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

12.3.1. Study Phases

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

Study Phase	Definition
Pre-Treatment	Date ≤ Study Treatment Start Date/Time
Treatment Emergent	Date > Study Treatment Start Date/Time

12.3.1.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is prior to study treatment
Concomitant	Any medication that is not a prior

NOTES:

- Please refer to Appendix 6: Reporting Standards for Missing Data for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

12.3.2. Treatment Emergent Flag for Adverse Events

Adverse Events will be flagged as Treatment Emergent as described in the table in Section 12.3.1, where the AE Start Date/Time will be considered.

12.4. Appendix 4: Data Display Standards & Handling Conventions

12.4.1. Reporting Process

Software

- The currently supported versions of SAS software will be used.

Reporting Area

HARP Server : \\uk1salx00175.corpnet2.com

HARP Compound

Reporting effort (RE) name in RAP	Type	HARP folder / RE name
Unplanned IA	Interim analysis	internal_01, internal_02
SAC	Pre-programming/ dry run	data_look_01, data_look_02
SAC	Final	final_01

Analysis Datasets

- Analysis datasets will be created according to Integrated Data Standards Library (IDSL) GSK A&R dataset standards.

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
- 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

- All data will be reported according to the actual treatment the participant received.
- 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.
- Dates will be reported in the format DDMMMCCYY e.g. 01Jan2020 unless otherwise stated.

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 be included in summary tables and figures. Assessment windows for the unscheduled and early withdrawal assessments are specified in Appendix 2: Assessment Windows. • 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, % N = the number of participants from the relevant analysis population for the group or subgroup. n = the number of participants counted for the summary statistic.

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: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.
PC Windows Non-Linear (WNL) File for GSK2330811	PC WNL file (CSV format) for the non compartmental analysis by Clinical Pharmacology Modelling and Simulation function will be created according to GUI_51487. Note: Concentration values will be imputed as per GUI_51487. Note: GSK2330811 concentration values will be imputed as per GUI_51487.
Pharmacokinetic Parameter Derivation	
PK Parameter to be Derived by Programmer	None
Pharmacokinetic Parameter Data	
Is NQ impacted PK Parameters Rule Being Followed	Yes, refer to SOP_314000.. If one or more non-quantifiable (NQ) values occur in a profile before the first measurable concentration, they will be assigned a value of zero concentration. For linear plots, zero concentration value(s) before the first measurable concentration will be included in the plot. For log-linear plots, zero concentration value(s) before the first measurable concentration will be assigned a missing value. If a single NQ value occurs between measurable concentrations in a profile, the NQ should generally be omitted (set to missing) in the derivation of pharmacokinetic parameters, statistical analysis, and the individual subject plots. If two or more NQ values occur in succession between measurable concentrations, the profile will be deemed to have terminated at the last measurable concentration prior to these NQs. For the purpose of individual subject plots, these NQs will be set to 0, and the subsequent measurable concentrations will be retained. For the

	derivation of pharmacokinetic parameters, these NQs and any subsequent measurable concentrations will be omitted (set to missing). NQs which occur after the last measurable concentration will be omitted (set to missing) in the derivation of pharmacokinetic parameters and from the individual subject plots. In some circumstances, there may be a pharmacokinetic rationale for fluctuation resulting in non-measurable concentrations in the middle of the concentration-time profile (e.g., entero-hepatic recycling, erratic absorption from transdermal/inhaled formulations). In these cases, the NQ values could be set to missing or to some other values (e.g., ½ LLQ) and subsequent valid concentrations may be retained. A reference line indicating LLQ will be included in plots. For the calculation of mean or median pharmacokinetic profiles. When estimating the mean or median value for the concentration at a given time point (i.e., descriptive mean or median curve), the following guidelines should be considered: All NQ values will be set to zero except when an individual NQ falls between two quantifiable values, in which case it will be omitted from the calculation of mean or median profiles. Measurable concentrations which follow more than one consecutive mid-profile NQ will be omitted (set to missing). The mean/median value at a time-point where one or more samples have NQ values will be reported (in tabular or graphical fashion) even if the mean/median value is below the LLQ of the assay. For linear plots, zero concentration value(s) will be included in the plot. For log-linear plots, zero concentration value(s) will be assigned a missing value. Zero mean or median values will be included in summary tables. In certain cases, the NQ values could be set to missing or to some other values (e.g., ½ LLQ) with proper scientific justification(s). A reference line indicating LLQ will be included in plots. It should be noted that a high proportion of NQ values may affect the standard deviation (SD); if more than 30% of values are imputed, then SD will not be displayed. Any table of summary statistics for concentration-time data will report N (number of subjects in the analysis population), n (number of subjects with non-missing values) and number imputed (number of subjects with imputed values (i.e., NQ assigned zero concentration). BQL (Below the Quantification Limit) may be displayed in listings by legacy systems instead of NQ; these abbreviations are interchangeable and mean that a sample has been received, analysed and a concentration below the LLQ of the assay found. Scientific judgement and prior knowledge should always be used in applying these guidelines.
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Refer to GUI_51487

12.4.4. Reporting Standards for Target Engagement

Total OSM Concentration Data	
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Refer to IDSL Statistical Principle 6.06.1. Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.
PC Windows Non-Linear (WNL) File for Total OSM	PC WNL file (CSV format) for the non compartmental analysis by Clinical Pharmacology Modelling and Simulation function will be created according to GUI_51487. Note: Total OSM concentration values will be imputed as per GUI_51487.
Total OSM Parameter Derivation	
Total OSM Parameter to be Derived by Programmer	None
Total OSM Parameter Data	
Is NQ impacted Total OSM Parameters Rule Being Followed	Yes, refer to SOP_314000. If one or more non-quantifiable (NQ) values occur in a profile before the first measurable concentration, they will be assigned a value of zero concentration. For linear plots, zero concentration value(s) before the first measurable concentration will be included in the plot. For log-linear plots, zero concentration value(s) before the first measurable concentration will be assigned a missing value. If a single NQ value occurs between measurable concentrations in a profile, the NQ should generally be omitted (set to missing) in the derivation of total OSM parameters, statistical analysis, and the individual subject plots. If two or more NQ values occur in succession between measurable concentrations, the profile will be deemed to have terminated at the last measurable concentration prior to these NQs. For the purpose of individual subject plots, these NQs will be set to 0, and the subsequent measurable concentrations will be retained. For the derivation of total OSM parameters, these NQs and any subsequent measurable concentrations will be omitted (set to missing). NQs which occur after the last measurable concentration will be omitted (set to missing) in the derivation of pharmacokinetic parameters and from the individual subject plots. For the calculation of mean or median total OSM profiles. When estimating the mean or median value for the concentration at a given time point (i.e., descriptive mean or median curve), the following guidelines should be considered: All NQ values will be set to zero except when an individual NQ falls between two quantifiable values, in which case it will be omitted from the calculation of mean or median profiles. Measurable concentrations which follow more than one consecutive mid-profile NQ will be omitted (set to missing). The mean/median value at a time-point where one or more samples have NQ values will be reported (in tabular or graphical fashion) even if the mean/median value is below the LLQ of the assay. For linear plots, zero concentration value(s) will be included in the plot. For log-linear plots, zero concentration value(s) will be assigned a missing value. Zero mean or median values will be included in summary tables. In certain cases, the NQ values could be set to missing or to some other values (e.g., ½ LLQ) with proper scientific justification(s). A reference line indicating LLQ will be included in plots. It should be noted that a high proportion of NQ values may affect the standard deviation (SD); if more than 30% of values are imputed, then SD will not be displayed.

	Any table of summary statistics for concentration-time data will report N (number of subjects in the analysis population), n (number of subjects with non-missing values) and number imputed (number of subjects with imputed values (i.e., NQ assigned zero concentration). BQL (Below the Quantification Limit) may be displayed in listings by legacy systems instead of NQ; these abbreviations are interchangeable and mean that a sample has been received, analysed and a concentration below the LLQ of the assay found. Scientific judgement and prior knowledge should always be used in applying these guidelines.
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Refer to GUI_51487

12.5. Appendix 5: Derived and Transformed Data

12.5.1. General

Multiple Measurements at One Analysis Time Point
• Where multiple assessments are made, the mean of replicate assessments at any given time point will be used as the value for that time point. This derived mean will be reported in the listing in addition to the individual assessments. • 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. • 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 Dose Date:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < Dose Date → Study Day = Ref Date – Dose Date
  • Ref Data ≥ Dose Date → Study Day = Ref Date – (Dose Date) + 1

12.5.2. Study Population

Cumulative Dose
Placebo: 0 GSK2330811: Number of Injections x 150 Dose unit: Milligram
Demographics
Age
• Only birth year is captured on the eCRF, therefore GSK standard ISDL algorithms will be used for calculating age where birth date will be imputed as follows: • The missing date and month will be imputed as '30th June' • Birth date will be presented in listings as 'YYYY'
Body Mass Index (BMI)
• Calculated as Weight(kg)/Height(m)^2

12.5.3. Safety

ECG Parameters
RR Interval
If RR interval (msec) is not provided directly, then RR can be derived using machine read QTcF as: $$RR = \left[\left(\frac{QT}{QTcF}\right)^3\right] * 1000$$

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 decimal places 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 places: '< x' becomes x – 0.01 o Example 2: 1 decimal places: '> x' becomes x + 0.1 o Example 3: 0 decimal places: '< x' becomes x – 1.

12.6. Appendix 6: Reporting Standards for Missing Data

12.6.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion (i.e. as specified in the protocol) was defined as completion of all assessment on Day 126. • A maximum of 4 non-evaluable participants will be replaced. • 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 or will be summarised as withdrawal visits.

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 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.
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	• In case of partial dates (i.e. day missing, only month and year present) recorded for AE start and end, 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: 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. • 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 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.

12.6.2.2. Imputation of Missing Data for OSM Free and Total

Element	Reporting Detail
LLQ/2	• If data are missing due to readings being below the limits of quantification, then a value equivalent to LLQ/2 will be imputed. • If the readings are above the upper limit of quantification, the sample should be further diluted to be within the upper limit of quantification of the assay. The measured concentration should then be corrected for the additional dilution factor. • These values will be used for the computation of the change from baseline and for summaries, plots and analysis, if deemed applicable. • The number of data imputed will be highlighted in the summaries and figures, whereas listings will report the values as below LLQ. • The numeric values and LLQ will be presented in listing as a reference, and the LLQ will be mentioned in footnotes where appropriate (e.g. figures).

12.7. Appendix 7: Values of Potential Clinical Importance

12.7.1. Laboratory Values

Haematology and chemistry parameters will use CTCAE grades (CTCAE criteria, V5.0: November 27, 2017) to highlight important results based on laboratory value only (i.e. no clinical judgement will be applied). CTCAE grades will replace the category of "values of potential clinical importance" for haematology parameters, see table below for reference.

Laboratory Parameter	CTCAE v5.0 Term for Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Haemoglobin	Anemia	Hemoglobin (Hgb) <LLN - 100 g/L	Hgb <100 - 80g/L	Hgb <80 g/L; transfusion indicated	Life-threatening consequences; urgent intervention indicated	Death
Haemoglobin	Hemoglobin increased	Increase in >0 - 2 g/dL above ULN or above baseline if baseline is above ULN	Increase in >2 - 4 g/dL above ULN or above baseline if baseline is above ULN	Increase in >4 g/dL above ULN or above baseline if baseline is above ULN	-	-
Lymphocyte count	Lymphocyte count decreased	<LLN - 0.8 GI/L	<0.8 - 0.5 GI /L	<0.5 - 0.2 GI /L	<0.2 GI /L	-
Lymphocyte count	Lymphocyte count increased	-	>4 – 20 GI/L	>20 GI/L	-	-
Neutrophil count	Neutrophil count decreased	<LLN - 1.5 GI /L	<1.5 - 1.0 GI /L	<1.0 - 0.5 GI /L	<0.5 GI/L	-
Platelet count	Platelet count decreased	<LLN - 75.0 GI /L	<75.0 - 50.0 GI /L	<50.0 - 25.0 GI /L	<25.0 GI/L	-
White blood cell count	Leukocytosis	-	-	>100 GI/L	Clinical manifestations of leucostasis; urgent intervention indicated	Death
White blood cell count	White blood cell	<LLN - 3.0 GI /L	<3.0 - 2.0 GI /L	<2.0 - 1.0 GI /L	<1.0 GI /L	-

Laboratory Parameter	CTCAE v5.0 Term for Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
	decreased					
Alanine Amino Transferase (IU/L)	Alanine aminotransferase increased	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	
Aspartate Amino Transferase (IU/L)	Aspartate aminotransferase increased	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	
Calcium (MMOL/L)	Hypocalcemia	Corrected serum calcium of <LLN - 2.0 mmol/L; Ionized calcium <LLN - 1.0 mmol/L	Corrected serum calcium of <2.0 - 1.75 mmol/L; Ionized calcium <1.0 - 0.9 mmol/L; symptomatic	Corrected serum calcium of <1.75 - 1.5 mmol/L; Ionized calcium <0.9 - 0.8 mmol/L; hospitalization indicated	Corrected serum calcium of; <1.5 mmol/L; Ionized calcium <0.8 mmol/L; life-threatening consequences	Death
Cholesterol	Cholesterol - high	>ULN - 7.75 mmol/L	>7.75 - 10.34 mmol/L	>10.34 - 12.92 mmol/L	>12.92 mmol/L	
Creatinine	Creatinine increased	>ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 x baseline; >3.0 - 6.0 x ULN	>6.0 x ULN	
Glucose	Hyperglycemia	Abnormal glucose above baseline with no medical intervention	Change in daily management from baseline for a diabetic; oral antiglycemic agent initiated;	Insulin therapy initiated; hospitalization indicated	Life-threatening consequences; urgent intervention indicated	Death

Laboratory Parameter	CTCAE v5.0 Term for Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
			workup for diabetes			
Glucose	Hypoglycemia	<LLN - 3.0 mmol/L	<3.0 - 2.2 mmol/L	<2.2 - 1.7 mmol/L	<1.7 mmol/L; life threatening consequences; seizures	Death
Potassium	Hyperkalemia	>ULN - 5.5 mmol/L	>5.5 - 6.0 mmol/L; intervention initiated	>6.0 - 7.0 mmol/L; hospitalization indicated	>7.0 mmol/L; life-threatening consequences	Death
Potassium	Hypokalemia	<LLN - 3.0 mmol/L	Symptomatic with <LLN - 3.0mmol/L; intervention indicated	<3.0 - 2.5 mmol/L; hospitalization indicated	<2.5 mmol/L; life-threatening consequences	Death
Sodium	Hypernatremia	>ULN - 150 mmol/L	>150 - 155 mmol/L; intervention initiated	>155 - 160 mmol/L; hospitalization indicated	>160 mmol/L; life-threatening consequences	Death
Sodium	Hyponatremia	<LLN - 130 mmol/L	125-129 mmol/L and asymptomatic	125-129 mmol/L symptomatic; 120-124 mmol/L regardless of symptoms	<120 mmol/L; life-threatening consequences	Death
Total Bilirubin	Blood bilirubin increased	>ULN - 1.5 x ULN if baseline was normal; > 1.0 - 1.5 x baseline if baseline was abnormal	>1.5 - 3.0 x ULN if baseline was normal; >1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 10.0 x ULN if baseline was normal; >3.0 - 10.0 x baseline if baseline was abnormal	>10.0 x ULN if baseline was normal; >10.0 x baseline if baseline was abnormal	Death
Triglycerides	hypertriglyceridemia	1.71 mmol/L - 3.42 mmol/L	>3.42 mmol/L - 5.7 mmol/L	>5.7 mmol/L - 11.4 mmol/L	>11.4 mmol/L; life-threatening consequences	Death

12.7.2. Laboratory Values – Haematology, Chemistry and Liver

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Hematocrit	Ratio of 1	Male		0.54
		Δ from BL	↓0.075	
Hemoglobin	g/L	Male		180
		Δ from BL	↓25	
Lymphocytes	$x10^9$/ L		0.8	
Neutrophil Count	$x10^9$/ L		1.5	
Platelet Count	$x10^9$/ L		100	550
While Blood Cell Count (WBC)	$x10^9$/ L		3	20

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Albumin	g/L		30	
Calcium	mmol/L		2	2.75
Creatinine	umol/L			>1.3*ULN
Creatinine		Δ from BL		↑ 44.2
Glucose	mmol/L		3	9
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150

Liver Function			
Test Analyte	**Units**	**Category**	**Clinical Concern Range**
ALT/SGPT	U/L	High	≥ 2x ULN
AST/SGOT	U/L	High	≥ 2x ULN
AlkPhos	U/L	High	≥ 2x ULN
T Bilirubin	µmol/L	High	≥ 1.5x ULN
T. Bilirubin + ALT	µmol/L U/L	High	1.5x ULN T. Bilirubin + ≥ 2x ULN ALT

12.7.3. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec		> 450
Absolute PR Interval	msec	< 110	> 220
Absolute QRS Interval	msec	< 75	> 110
Change from Baseline			
Increase from Baseline QTc	msec		> 60

12.7.4. Vital Signs

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

Vital Sign Parameter (Change from Baseline)	Units	Clinical Concern Range			
		Decrease		Increase	
		Lower	Upper	Lower	Upper
Systolic Blood Pressure	mmHg	≥ 20	≥ 40	≥ 20	≥ 40
Diastolic Blood Pressure	mmHg	≥ 10	≥ 20	≥ 10	≥ 20
Heart Rate	bpm	≥ 15	≥ 30	≥ 15	≥ 30

12.8. Appendix 8: Abbreviations & Trademarks

12.8.1. Abbreviations

Abbreviation	Description
AE	Adverse Event
AUC	Area Under the Curve
A&R	Analysis and Reporting
CI	Confidence Interval
CL/F	Apparent Clearance
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSR	Clinical Study Report
DBF	Database Freeze
DBR	Database Release
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Record Form
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
IP	Investigational Product
LLN	Lower Limit of Normal
NCA	Non-Compartmental Analysis
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
SAC	Statistical Analysis Complete
SOP	Standard Operation Procedure
TA	Therapeutic Area
TFL	Tables, Figures & Listings
tlast	Time of last quantifiable concentration
Tmax	Time of occurrence of Cmax
t1/2	Half-life
ULN	Upper Limit of Normal
Vss/F	Steady state apparent volume of distribution
%AUCex	Percentage of AUC(0-inf) obtained by extrapolation

12.8.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
None

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS
WinNonlin

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 1.11	
Safety	3.1 to 3.23	3.1 to 3.5
Pharmacokinetic	4.1 to 4.3	4.1 to 4.3
Pharmacodynamic and / or Biomarker	6.1 to 6.6	6.1 to 6.3
Pharmacokinetic / Pharmacodynamic		7.1
Section	**Listings**	
ICH Listings	1 to 27	
Other Listings	28 to 35	

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
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Pharmacodynamic and / or Biomarker	PD_Fn	PD_Tn	PD_Ln
Pharmacokinetic / Pharmacodynamic	PKPD_Fn	PKPD_Tn	PK/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 [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 [Priority]**
Subject Disposition					
1.1.	Safety	ES1	Summary of Subject Disposition	Include total column	SAC
1.2.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure		SAC
Protocol Deviation					
1.3.	Safety	DV1	Summary of Important Protocol Deviations Not Related to COVID-19		SAC
1.4.	Safety	DV1	Summary of Important Protocol Deviations Related to COVID-19		
Population Analysed					
1.5.	Screened	SP1	Summary of Study Populations		SAC
Demography					
1.6.	Safety	DM1	Summary of Demographic Characteristics	Include: Height, Weight, and BMI	SAC
1.7.	Enrolled	DM11	Summary of Age Ranges		SAC
1.8.	Safety	DM6	Summary of Race and Racial Combinations		SAC
Concomitant Medications and other Medical Conditions					
1.9.	Safety	MH4	Summary of Past Medical Conditions		SAC
1.10.	Safety	MH4	Summary of Current Medical Conditions		SAC
1.11.	Safety	CM8	Summary of Concomitant Medications		SAC

12.9.5. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	Safety	AE1	Summary of All Adverse Events by System Organ Class and Preferred Term		SAC
3.2.	Safety	AE5A	Summary of Adverse Events by System Organ Class and Preferred Term and Maximum Intensity		SAC
3.3.	Safety	AE1	Summary of Drug-Related Adverse Events by System Organ Class and Preferred Term		SAC
3.4.	Safety	AE15	Summary of Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC
Serious and Other Significant Adverse Events					
3.5.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC
3.6.	Safety	AE3	Summary of Serious Drug-Related Adverse Events by Overall Frequency		SAC
3.7.	Safety	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term		SAC
Chemistry					
3.8.	Safety	LB1	Summary of Chemistry		SAC
3.9.	Safety	LB17	Summary of Worst-Case Chemistry Results Relative to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline		SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.10.	Safety	SAFE_T1	Summary of Chemistry Results by Maximum CTCAE Grade	Footnote: "CTCAE criteria, V5.0: November 27, 2017"	SAC
Haematology					
3.11.	Safety	LB1	Summary of Haematology	By parameter	SAC
3.12.	Safety	LB16	Summary of Haematology Results by Maximum CTCAE Grade Increase Post-Baseline Relative to Baseline	Footnote: "CTCAE criteria, V5.0: November 27, 2017"	SAC
3.13.	Safety	LB17	Summary of Worst Case Haematology Results Relative to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline		SAC
3.14.	Safety	SAFE_T2	Summary of Nadirs for Selected Haematology Parameters	By parameter, treatment group Produce for Platelet count and Haemoglobin. Footnote: "Nadir is the lowest post-baseline value of the parameter"	SAC
3.15.	Safety	SAFE_T3	Summary of Days to Nadir of Selected Haematology Parameters	by parameter, treatment group. Produce for Platelet count and Haemoglobin. Footnote: "Nadir is the lowest post-baseline value of the parameter"	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Urinalysis					
3.16.	Safety	SAFE_T4	Summary of Worst Case Urinalysis Results Post-Baseline Relative to Baseline	Tests to include: Urine blood, Urine Glucose (dipstick), Urine Ketones (dipstick), Urine Microscopy – Bacteria, Urine Microscopy - Red Blood Cells, Urine Microscopy - White Blood Cells, Urine Protein (dipstick), Urine Specific Gravity	SAC
ECG					
3.17.	Safety	EG1	Summary of ECG Findings		SAC
3.18.	Safety	EG2	Summary of ECG Values	Footnote: Average used for triplicate ECG measurements	SAC
3.19.	Safety	EG2	Summary of Change from Baseline in ECG Values	Footnote: Average used for triplicate ECG measurements	SAC
Vital Signs					
3.20.	Safety	VS1	Summary of Change from Baseline in Vital Signs		SAC
3.21.	Safety	VS7	Summary of Worst Case Vital Signs Results Relative to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline		SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.22.	Safety	SAFE_T5	Summary of Worst Case Vital Sign Results Relative to Change from Baseline Potential Clinical Importance (PCI) Criteria		SAC
Immunogenicity					
3.23.	Safety	IMM1	Occurrence of Anti-Drug Antibodies	Add footnote: Note: The denominator for confirmed positive is the total number of subjects at that visit who have immunogenicity data available.	SAC

12.9.6. Safety Figures

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Haematology					
3.1.	Safety	SAFE_F1	Subject Profiles for Haematology by Treatment Group	By Haematology parameter. This output should be produced for: Platelet Count, Haemoglobin Use rules for CTCAE boundaries X axis use 'Actual Relative Time (Days)' from dose. Show all observed values including unscheduled. Add footnote "Figure displays a subset of haematology parameters" Panel by treatment group	SAC
3.2.	Safety	SAFE_F2	Mean Profile for Haematology by Treatment Group	By Haematology parameter. This output should be produced for: Platelet Count, Haemoglobin X axis shows visits with approximate temporal spacing Add footnote "Figure displays a subset of haematology parameters"	SAC
3.3.	Safety	SAFE_F3	LFT Patient Profiles	ALT = Alanine Amino Transferase, AST = Aspartate Amino Transferase, Alk. Phos. = Alkaline Phosphatase,Total Bili. = Total Bilirubin	SAC
ECG					
3.4.	Safety	EG7	Empirical Distribution Function for Maximum Change from baseline in QTcF Interval	Both treatments in one plot. Calculate maximum change from baseline.	SAC

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.5.	Safety	EG8	Distribution of QTcF Change by Visit and Treatment	Use the 0, 30, 60 thresholds following shell.	SAC

12.9.7. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration					
4.1.	PK	PKCT1	Summary of Plasma GSK2330811 Concentration-Time Data	Note: LLQ=100 ng/mL. Values below LLQ have been imputed to 0. SD is set to missing if No. Imputed/n > 0.3 .	SAC
Derived PK parameters					
4.2.	PK	PKPT1	Summary of Derived Plasma Pharmacokinetic Parameters of GSK2330811		SAC
4.3.	PK	PKPT3	Summary of Log-Transformed Derived Plasma Pharmacokinetic Parameters of GSK2330811		SAC

12.9.8. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration					
4.1.	PK	PKCF1P	Individual GSK2330811 Plasma Concentration-Time Plot by Subject (Linear and Semi-Log)	Footnote for all PK and PK/PD figures: 'LLQ is calculated at 100 ng/mL. Values below LLQ have been imputed to 0.' Use actual time (days) as x axis (where days is a continuous variable)	SAC
4.2.	PK	PKCF4	Mean (±SD) Plasma GSK2330811 Concentration-Time Plots by Treatment (Linear and Semi-log)	Use planned time (days) as x axis (where days is a continuous variable)	SAC
4.3.	PK	PKCF5	Median (Range) Plasma GSK2330811 Concentration-Time Plots by Treatment (Linear and Semi-log)	Use planned time (days) as x axis (where days is a continuous variable)	SAC

12.9.9. Pharmacodynamic (and / or Biomarker) Tables

Pharmacodynamic (and or Biomarker): Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Serum level of OSM					
6.1.	Safety	PD1	Summary of Serum Level of Free OSM by Treatment Group	Calculate confidence intervals and add number imputed Add footnote: [1] No. of subjects with BLQs assigned half of the lower limit of quantification **(LLQ = 2.5pg/ml)**	SAC
6.2.	Safety	PD1	Summary of Serum Level of Total OSM by Treatment Group	Calculate confidence intervals and add number imputed Add footnote: [1] No. of subjects with BLQs assigned half of the lower limit of quantification **(LLQ = 2.5pg/ml)**	SAC
6.3.	Safety	PD1	Summary of Ratio of Serum Level of Total OSM to Baseline by Treatment Group	Calculate confidence intervals and add number imputed Add footnote: [1] No. of subjects with BLQs assigned half of the lower limit of quantification **(LLQ = 2.5pg/ml)**	SAC
6.4.	Safety	PD2	Summary of Log Transformed Serum Level of Total OSM by Treatment Group	Calculate confidence intervals and add number imputed Add footnote: [1] No. of subjects with BLQs assigned half of the lower limit of quantification **(LLQ = 2.5pg/ml)**	SAC

Pharmacodynamic (and or Biomarker): Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.5.	Safety	PKPT1	Summary of Derived Serum Pharmacokinetic Parameters of Total OSM by Treatment Group		SAC
6.6.	Safety	PKPT3	Summary of Log-Transformed Derived Serum Pharmacokinetic Parameters of Total OSM by Treatment Group		SAC

12.9.10. Pharmacodynamic (and / or Biomarker) Figures

Pharmacodynamic (and or Biomarker): Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Serum levels of OSM					
6.1.	Safety	PKCF1P	Individual Serum Level of Total OSM Concentration-Time Plot by Treatment (Linear and Semi-Log)	Add LLQ reference line Conditionally add ULQ reference line Page by treatment Total OSM: LLQ is calculated at 2.5pg/ml. Values below LLQ have been imputed to LLQ/2. Use actual time (days) as x axis (where days is a continuous variable) Add Footnote to indicate amount of imputed data.	SAC
6.2.	Safety	PKCF4	Mean (±SD) Serum Level of Total OSM Concentration-Time Plots by Treatment (Linear and Semi-log)	Add LLQ reference line Conditionally add ULQ reference line Use planned time (days) as x axis (where days is a continuous variable) Total OSM: LLQ is calculated at 2.5pg/ml. Values below LLQ have been imputed to LLQ/2.	SAC
6.3.	Safety	PKCF5	Median (Range) Serum Level of Total OSM Concentration-Time Plots by Treatment (Linear and Semi-log)	Add LLQ reference line Conditionally add ULQ reference line Use planned time (days) as x axis (where days is a continuous variable) Total OSM: LLQ is calculated at 2.5pg/ml. Values below LLQ have been imputed to LLQ/2.	SAC

12.9.11. Pharmacokinetic / Pharmacodynamic Figures

Pharmacokinetic / Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
OSM vs GSK2330811 concentration					
7.1.	PK	PKPD_F1	Scatter Plot of Total Serum OSM vs Plasma Concentration of GSK2330811	X axis: PK Page by visit Add LLQ reference lines for both Conditionally add ULQ reference line for total Footnotes: GSK2330811: LLQ is calculated at 100 ng/mL. Values below LLQ have been imputed to 0. Total OSM: LLQ is calculated at 2.5pg/ml. Values below LLQ have been imputed to LLQ/2.	SAC

12.9.12. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Screened	ES7	Listing of Reasons for Screen Failure		SAC
2.	Enrolled	ES2	Listing of Reasons for Study Withdrawal		SAC
3.	Enrolled	BL1	Listing of Subjects for Whom the Treatment Blind was Broken		SAC
4.	Enrolled	TA1	Listing of Planned and Actual Treatments		SAC
Protocol Deviations					
5.	Enrolled	DV2	Listing of Important Protocol Deviations		SAC
6.	Enrolled	DV2	Listing of COVID-19 related Protocol Deviations		SAC
7.	Enrolled	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC
Populations Analysed					
8.	Enrolled	SP3	Listing of Subjects Excluded from Any Population		SAC
Demography					
9.	Enrolled	DM2	Listing of Demographic Characteristics		SAC
10.	Enrolled	DM9	Listing of Race		SAC
Prior and Concomitant Medications					
11.	Enrolled	CM3	Listing of Concomitant Medications		SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure and Treatment Compliance					
12.	Enrolled	EX3	Listing of Exposure Data	Order by treatment, subject r. Include: Treamtent, Site ID/subjID, Start Datetime of Dose/Study day, Stop Datetime of Dose/Study day, Dose (this will be the cumulative dose) (eg450), Dose units, Root of administration, Number of injections	SAC
Adverse Events					
13.	Enrolled	AE8	Listing of All Adverse Events		SAC
14.	Enrolled	AE7	Listing of Subject Numbers for Individual Adverse Events		SAC
15.	Enrolled	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text		SAC
Serious and Other Significant Adverse Events					
16.	Enrolled	AE8CP	Listing of Serious Adverse Events		SAC
17.	Enrolled	AE14	Listing of Reasons for Considering as a Serious Adverse Event		SAC
18.	Enrolled	AE8CP	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment		SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Haematology					
19.	Enrolled	SAFE_L1	Listing of All Haematology Values and Changes from Baseline	See listing 23 in 201246. Report: Standard result, Change from baseline and Percent change from baseline. Do not flag CTCAE grades	SAC
20.	Enrolled	LB5	Listing of Laboratory Values of CTCAE Grade	Include Haematology and clinical chemistry laboratory data	SAC
21.	Enrolled	LB5	Listing of All Laboratory Data for Subjects with Any Value of Potential Clinical Importance	Include Haematology and clinical chemistry laboratory data	SAC
22.	Enrolled	LB14	Listing of Laboratory Data with Character Results		SAC
Urinalysis					
23.	Enrolled	UR2	Listing of Urinalysis Results		SAC
ECG					
24.	Enrolled	EG3	Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance		SAC
25.	Enrolled	EG5	Listing of Abnormal ECG Findings		SAC
Vital Signs					
26.	Enrolled	VS4	Listing of All Vital Signs Data for Subjects with Any Value of Potential Clinical Importance		SAC
Immunogenicity					
27.	Enrolled	IMM2	Listing of Immunogenicity Results		SAC

12.9.13. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK concentration and derived PK parameters					
28.	PK	PKCL1	Listing of GSK2330811 Plasma Concentration-Time Data	Add data dependent footnote: 'Note: NA=Not Available [data dependent], NQ=Non-Quantifiable, LLQ value=100ng/mL'	SAC
29.	PK	PKCL1	Listing of Derived GSK2330811 Pharmacokinetic Parameters		SAC
Serum levels of OSM					
30.	PK	PKCL1	Listing of Serum Level of OSM	Include both Free and Total OSM Add footnote: 'Note: BLQ = Below the limit of quantification which is 2.5pg/ml for both free and total OSM'	SAC
31.	Safety	PKCL1	Listing of Derived Total OSM Pharmacokinetic Parameters		SAC
Serum levels of TPO and EPO					
32.	PK	PKCL1	Listing of Level of Thrombopoietin in Serum		SAC
33.	PK	PKCL1	Listing of level of Erythropoietin in Plasma		SAC
Other					
34.	Enrolled	PAN12	Listing of COVID-19 Assessments and Symptom Assessments for Subjects with COVID-19 Adverse Events		SAC
35.	Enrolled	PAN7	Listing of All Subjects with Visits and Assessments Impacted by COVID-19 Pandemic		SAC

12.10. Appendix 10: Example Mock Shells for Data Displays

Example: SAFE_T1
Protocol: 208564 Page 1 of n
Population: Safety

Table XX.XX
Summary of Chemistry Results by Maximum CTCAE Grade

Test: Creatinine (UMOL/L)

Event: Creatinine increased

Treatment	N	Grade 1	Grade 2	Grade 3	Grade 4
Placebo	XX	XX	XX.X	XX.XX	XX.X
GSK2330811 450 mg	XX	XX	XX.X	XX.XX	XX.X

Note: CTCAE criteria, V5.0: November 17, 2017 graded on laboratory test value.

Only events with at least one graded value are shown.

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Example: SAFE_T2
Protocol: 208564 Page 1 of n
Population: Safety

Table XX.XX
Summary of Nadirs for Selected Haematology Parameters [as Percent Change from Baseline]

Lab Test (unit)	Treatment	N	n	Mean	SD	Median	Min	Max
Hemoglobin (G/L)	Placebo	XX	XX	XX.X	XX.XX	XX.X	XX.X	XX.X
	GSK2330811 450 mg	XX	XX	XX.X	XX.XX	XX.X	XX.X	XX.X

……

Note: Nadir is the lowest post-baseline value of the parameter.

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Example: SAFE_T3
Protocol: 208564
Population: Safety

Table XX.XX
Summary of Days to Nadir for Selected Haematology Parameters

Lab Test (unit)	Treatment	N	n	Median	Min	Max	Range
Hemoglobin (G/L)	Placebo	XX	XX	XX	XX	XX	XX
	GSK2330811 450 mg	XX	XX	XX	XX	XX	XX

……

Note: Nadir is the lowest post-baseline value of the parameter.

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Example: SAFE_T4

Programming note: please flag to study team/ statistics when summarizing if observe any character variables not the minimum value and not presented as an increase category.

Tests to summarise as X=BACTM_URQ (minimum value=NONE SEEN)
Tests to summarise as Y= BLD_URC, PROT_URG, KETO_URG, GLUC_URG (minimum value=NEGATIVE)
Tests to summarise as Z= RBCM_URG, WBCM_URG (minimum value=NONE SEEN)
Tests to summarise as W= SG_URG (minimum value=Low)

Example modified from UR1
Protocol: ABC123456
Population: Safety/Other study specific

Table X
Summary of Worst Case Urinalysis Results Post-Baseline Relative to Baseline

Test		Treatment A (N=248)	Treatment B (N=247)
X	n	230	232
	No Change/Decreased	222 (97%)	223 (96%)
	Any Increase	8 (3%)	9 (4%)
	Increase to MANY	6 (3%)	5 (2%)
Y	n	230	232
	No Change/Decreased	222 (96%)	222 (96%)
	Any Increase	7 (3%)	10 (4%)
	Increase to TRACE	2 (<1%)	5 (2%)
	Increase to 1+	1 (<1%)	4 (2%)
	Increase to 2+	1 (<1%)	0
	Increase to 3+	4 (2%)	1 (<1%)
Z	n	230	232
	No Change/Decreased	222 (96%)	222 (96%)
	Any Increase	7 (3%)	10 (4%)
	Increase to 0-1	2 (<1%)	5 (2%)
	Increase to 5-10	1 (<1%)	4 (2%)
	Increase to 10-15	1 (<1%)	0
	Increase to 15-20	2 (<1%)	1 (<1%)

		Increase to 20-25	2	(<1%)	0	
		Increase to 25-50	4	(2%)	1	(<1%)
W		n	230		232	
		No Change/Decreased	222	(97%)	223	(96%)
		Any Increase	8	(3%)	9	(4%)
		Increase to NORMAL	6	(3%)	5	(2%)
		Increase to HIGH	6	(3%)	5	(2%)

Note: Little n does not include Not done or No results.

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Example: SAFE_T5
Protocol: 208564
Population: Safety

Table 3.22
Summary of Worst Case Vital Sign Results Relative to Change from Baseline Potential Clinical Importance (PCI) Criteria

Test (Unit)	Change Category	Placebo (N=XX)	GSK2330811 450 mg (N=XX)
Diastolic blood pressure (mmHg)	n	xx	xx
	Decrease >= 10	xx (xx%)	xx (xx%)
	Decrease >= 20	xx (xx%)	xx (xx%)
	Increase >= 10	xx (xx%)	xx (xx%)
	Increase >= 20	xx (xx%)	xx (xx%)
Heart Rate (bmp)	n	xx	xx
	Decrease >= 15	xx (xx%)	xx (xx%)
	Decrease >= 30	xx (xx%)	xx (xx%)
	Increase >= 15	xx (xx%)	xx (xx%)
	Increase >= 30	xx (xx%)	xx (xx%)
Systolic blood pressure (mmHg)	n	xx	xx
	Decrease >= 20	xx (xx%)	xx (xx%)
	Decrease >= 40	xx (xx%)	xx (xx%)
	Increase >= 20	xx (xx%)	xx (xx%)
	Increase >= 40	xx (xx%)	xx (xx%)

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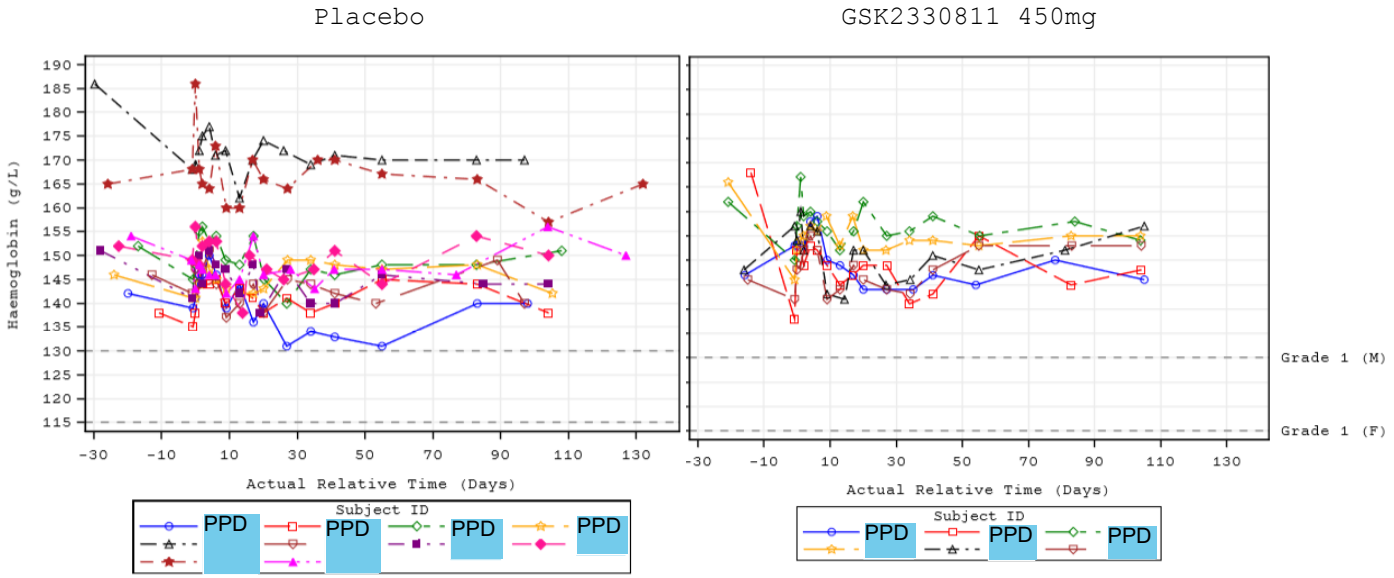
Example: SAFE_F1
Protocol: 208564
Population: Safety

Figure XX.XX
Participant Profiles for Haematology by Treatment Group



Programming notes:
One legend including all participants.
Make plot as large as possible to fill space.
add (P) to denote placebo participants.
y-axis will be displayed on the left-hand side plot and the labels for the reference lines will be included on the right-hand side plot.

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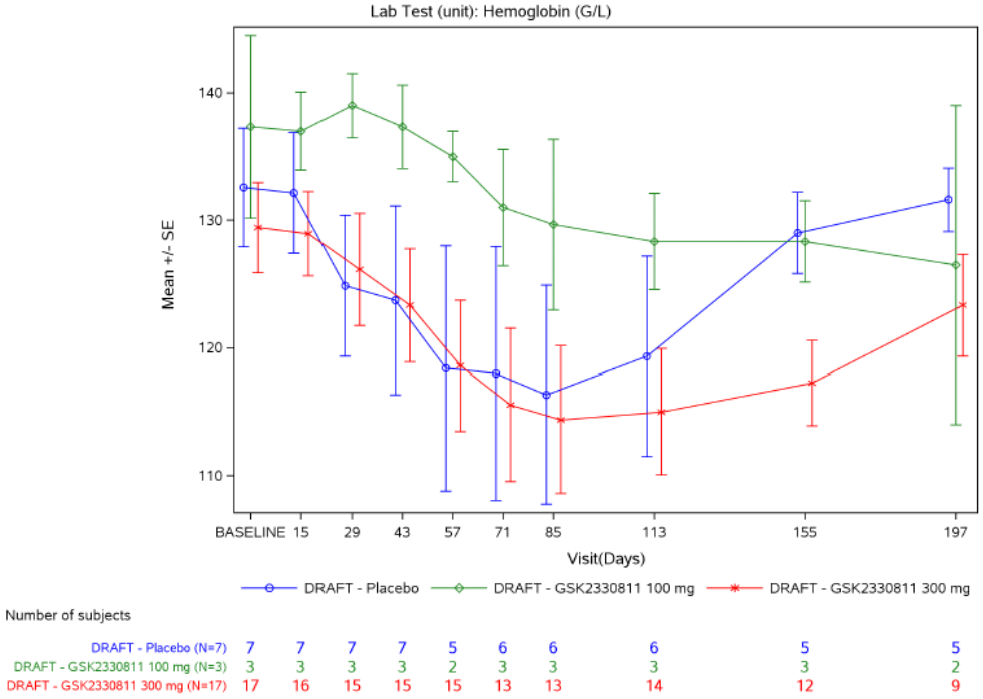
Example: SAFE_F2
Protocol: 208564
Population: Safety

Figure XX.XX
Mean Profile for Haematology by Treatment Group



Programming notes:
See output 3.9 from 201247.
Make plot as large as possible to fill space.
Use different marker symbol, line pattern and colour by treatment group.
Table: Include N after treatment group and use same colour as in the plot.

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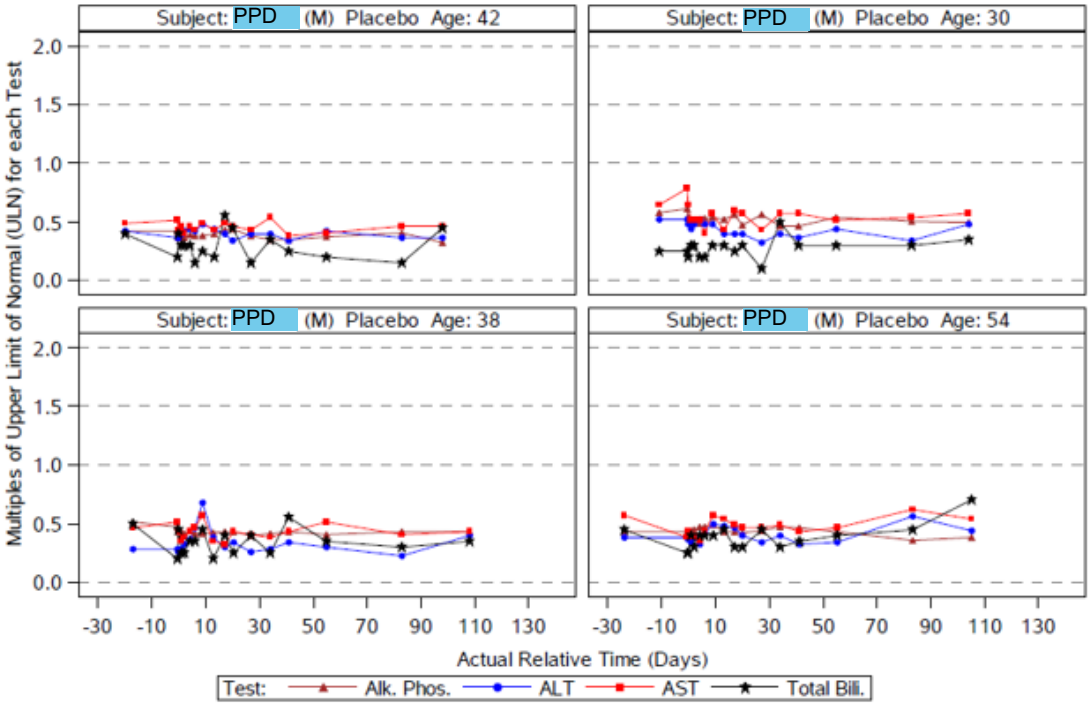
Example: SAFE_F3
Protocol: 208564
Population: Safety

Figure XX.XX
LTF Patient Profiles



Note: M = Male, F = Female, ALT = Alanine Amino Transferase, AST = Aspartate Amino Transferase, Alk. Phos. = Alkaline Phosphatase,Total Bili. = Total Bilirubin
Clinical Concern Levels: ALT, AST and Alk. Phos: 2 times respective ULN, Total Bili: 1.5 times the ULN

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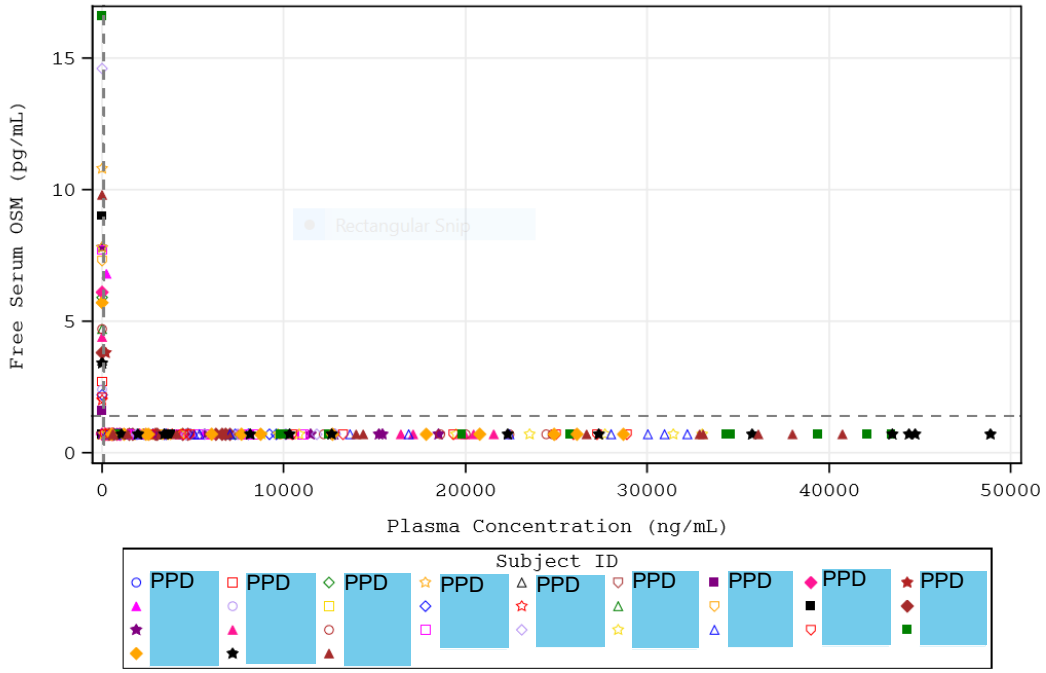
Example: PKPD_F1
Protocol: 208564
Population: PK

Figure XX.XX
Scatter Plot of Free Serum OSM vs Plasma Concentration of GSK2330811



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Example: SAFE_L1
Protocol: 208564
Population: Enrolled

Listing XX
Listing of All Haematology Values and Changes from Baseline

Lab Test (Units)	Treatment	CentreID/ subjid	Visit/Analysis visit	Date of collection	Study Day	Standard Result	Change from Baseline	Percentage Change from Baseline
xx		Xx/xx	xx	xx	xx	xx	xx	xx

Signature Page for 208564 TMF-7927164 v1.0

Reason for signing: Approved	Name: PPD Role: Approver Date of signature: 07-Dec-2020 08:33:02 GMT+0000

Reason for signing: Approved	Name: PPD Role: Approver Date of signature: 07-Dec-2020 14:00:17 GMT+0000

Signature Page for TMF-7927164 v1.0