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

Title	:	Reporting and Analysis Plan for A Phase I/II, Open-Label Study to Investigate the Safety, Clinical Activity, Pharmacokinetics, and Pharmacodynamics of GSK3145095 Administered Alone and in Combination with Anticancer Agents Including Pembrolizumab in Adult Participants with Selected Advanced Solid Tumors
Compound Number	:	GSK3145095
Effective Date	:	18-OCT-2019

Description:

- The purpose of this RAP is to describe the planned analyses and outputs to be included in the Synoptic Clinical Study Report for Protocol 205013.
- This RAP will be provided to the study team members to convey the content of the Part 1 Statistical Analysis Complete (SAC) deliverable. Due to early termination of the study, Part 2, Part 3 and Part 4 were not initiated. This document will only include the reporting plan for subjects enrolled in the study.
- Only the primary and secondary objectives are to be analysed due to the early termination.

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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:

Insert revision chronology as detailed within the protocol.

Revision Chronology:		
2017N343207_00	22-JUN-2018	Original Protocol
2017N343207_01	28-JUN-2018	Original Protocol (republished)
2017N343207_02	06-AUG-2018	Original Protocol (republished)
2013N343207_03	25-OCT-2018	Amendment 1 incorporates summary of changes to the protocol as requested by the United States Food and Drug Administration (FDA).

All data displays (Tables, Figures & Listings) will use the term "Subject" which reflects CDISC and GSK Data Display Standards terminology.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Due to the early termination of the study 205013 during part 1, this RAP is developed for a synoptic CSR. Subsequent parts were not initiated prior to study closure; therefore, no statistical outputs will be produced for Part 2, Part 3 and Part 4.

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

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	**Reporting & Analysis Plan**	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
• No changes or deviations specified in the protocol amendment 1 (Dated: 25/OCT/2018).	• No Statistical Analysis or outputs to be generated for Part 2, Part 3 and Part 4	• Part 2, Part 3 and Part 4 were not implemented
• Full CSR	• Synoptic CSR	• Early study termination during part 1.

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

Parts 1 & 2: Dose Escalation	
Objectives	**Endpoints**
Primary Objectives	**Primary Endpoints**
• To evaluate the safety and tolerability and identify the maximum tolerated dose (MTD) or the maximum acceptable dose (MAD) of GSK3145095 administered orally alone and in combination with other agents such as pembrolizumab to participants with selected advanced or recurrent solid tumors.	• Frequency and severity of adverse events including frequency of DLTs.
Secondary Objectives	**Secondary Endpoints**
• To evaluate the antitumor activity of GSK3145095 alone and in combination with other agents such as pembrolizumab in participants with selected advanced or recurrent solid tumors.	• Best overall response based on RECIST 1.1 criteria.
• To characterize the pharmacokinetics (PK) of GSK3145095 alone and in combination with other agents such as pembrolizumab in participants with selected advanced or recurrent solid tumors.	• Derived PK parameters for GSK3145095 including area under the plasma drug concentration versus time curve (AUC(0-t), AUC(0- τ)), maximum observed plasma drug concentration (Cmax), minimum observed plasma drug concentration (Cmin), time to maximum observed plasma drug concentration (tmax), clearance (CL/F), volume of distribution (V/F) and terminal half-life (t1/2) following single and repeat doses, and evaluation of dose proportionality, accumulation ratio and time invariance where data allow
• To characterize the pharmacokinetics (PK) of pembrolizumab when administered in combination with GSK3145095.	• Serum pembrolizumab concentrations and PK parameters including Cmax, AUC(0-τ), and Cmin.
Parts 3 & 4: Dose Expansion	
Objectives	**Endpoints**
Primary Objectives	**Primary Endpoints**
• To evaluate the antitumor activity of GSK3145095 in combination with other agents such as pembrolizumab in participants with selected advanced or recurrent solid tumors.	• Overall Response Rate (ORR; % of participants achieving CR or PR) based on RECIST 1.1 criteria.

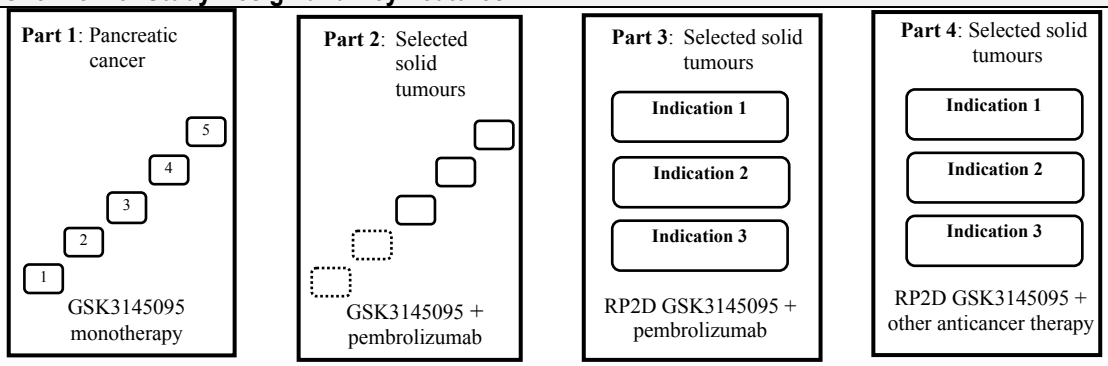
Secondary Objectives	Secondary Endpoints
• To further evaluate the safety and tolerability of GSK3145095 administered orally in combination with other agents such as pembrolizumab to participants with selected advanced or recurrent solid tumors.	• Frequency and severity of adverse events.
• To further evaluate the antitumor activity of GSK3145095 in combination with other agents such as pembrolizumab in participants with selected advanced or recurrent solid tumors.	• Progression-Free Survival and Overall Survival.
• To characterize the PK of GSK3145095 in combination with other agents such as pembrolizumab in participants with selected advanced or recurrent solid tumors.	• Derived PK parameters for GSK3145095 and combination agent including AUC(0-t), AUC(0-τ), Cmax, tmax, and t1/2 following single and repeat doses, and evaluation of dose proportionality, accumulation ratio and time invariance estimation of an accumulation ratio where data allow
Parts 1, 2,3, & 4: Exploratory Objectives	
Exploratory Objectives	**Exploratory Endpoints**
• To explore the inter-relationship between antitumor activity, PK parameters, pharmacodynamic activity, and other participant characteristics	• Assessment of antitumor activity (CR, PR, SD, progressive disease [PD]), tumor kinetic/PK parameters, pharmacodynamic activity, and other participant characteristics
• To evaluate the pharmacokinetic and pharmacodynamic activity of GSK3145095 in the periphery and the tumor microenvironment	• Assessment of GSK3145095 tumor penetration, RIP1 target engagement, activation, and pathway inhibition may be explored.
• To evaluate the relationship between GSK3145095 and safety parameters, including QTcB following single and repeated administration.	• Relationship between GSK3145095 exposure (e.g. concentration, Cmax, AUC) and safety parameters including change from baseline QTcF.
• To explore the effect of RIP1 inhibition on the tumor microenvironment and the immune response within the tumor and periphery	May include assessment of: • Tumor biopsies via immunohistochemistry (IHC) • Changes in gene expression (ribonucleic acid [RNA] and protein), T cell receptor [TCR] diversity, tumor microenvironment or mutational load (genomic deoxyribonucleic acid [DNA]) • Measures of immune function in peripheral blood mononuclear cells (PBMCs) • Expression of circulating soluble factors

• To investigate the mechanism of action and indicators of sensitivity and resistance to GSK3145095 alone or in combination with other agents such as pembrolizumab	• Assessment of DNA, RNA, and/or protein markers in tumor or periphery and their association with anti-tumor activity for potential use in the development of a predictive biomarker and/or diagnostic test
• To characterize the metabolite profile of GSK3145095 after single or repeated oral dosing in some participants	• Identification and quantitative estimates of parent GSK3145095 and metabolites in plasma and/or urine following single or repeat doses
• To assess potential effect of repeat doses of GSK3145095 on Cytochrome P450 3A4 (CYP3A4) enzyme activity in some participants	• Plasma 4βhydroxycholesterol to cholesterol ratio pre-treatment and following repeat dosing of GSK3145095
• To evaluate disease and treatment related symptoms and impact on function and health-related quality-of-life (Parts 3 & 4 only)	• Qualitative telephone interview(s)
• To investigate the relationship between genetic variants in candidate genes, PK, and safety profile of GSK3145095 alone or in combination with other agents such as pembrolizumab	• Pharmacogenomic (PGx) study using blood samples

Note that ECGs, vitals, labs (chem, haem and urinalysis), liver events are also incorporated in the safety reporting.

2.3. Study Design

Overview of Study Design and Key Features



Design Features	• This study consists of 4 parts; Parts 1 and 2 represent dose escalation while Parts 3 and 4 represent dose expansion. • Part 1 is designed to evaluate safety and tolerability of escalating doses of GSK3145095 alone in participants with advanced or metastatic pancreatic ductal adenocarcinoma (PDAC) using Neuenschwander-Continual Reassessment Method (N-CRM) design [Neuenschwander, 2008] to identify a dose for evaluation in Part 2. PK samples will be obtained to evaluate PK parameters. Initiation of Part 2 will occur after emerging data from Part 1 demonstrates the safety of GSK3145095 monotherapy. • Part 2 combines escalating doses of GSK3145095 with 200 mg pembrolizumab (fixed dose). Modified Toxicity Probability Interval (mTPI) (Ji 2013) will be used to identify the MTD of GSK3145095 in combination with pembrolizumab and determine the recommended dose for the dose expansion phase (Parts 3 and 4). Following protocol amendment, a broader population of selected solid tumours may be enrolled in part 2. These tumor types include PDAC, NSCLC, triple-negative breast cancer, and/or melanoma. Part 2 will begin with a GSK3145095 dose below the highest Part 1 dose shown to have an acceptable toxicity profile in at least 3 participants. • Part 3 dose expansion is designed to evaluate safety, PK, pharmacodynamic activity, and clinical activity of one or more doses of GSK3145095 in combination with 200 mg pembrolizumab. Any dose level(s) established as safe in Parts 1 or 2 may be selected for cohort expansion. All available safety, pharmacodynamic, PK, and efficacy data will be used to select one or more doses of GSK3145095 for cohort expansion. Part 3 will be opened via a protocol amendment • Part 4 dose expansion will investigate the combination of additional anticancer agent(s) with one or more doses of GSK3145095 identified as safe in Part 1. Part 4 will be opened via a protocol amendment.

Overview of Study Design and Key Features	
Dosing	• Part 1 will involve dose escalation of GSK3145095 starting with a 50mg dose administered orally (PO) twice daily (BID). Participants will receive a single dose of GSK3145095 PO on Day 1 with the BID schedule starting on Day 2. Four additional dose levels (ranging from 200 to 1600 mg) are planned. • Part 2 will involve dose escalation of GSK3145095 in combination with pembrolizumab beginning with a GSK3145095 dose below the highest Part 1 (monotherapy) dose shown to have an acceptable toxicity profile in at least 3 participants. The dose of pembrolizumab will remain fixed at 200 mg administered IV once every three weeks (Q3W). Part 2 will be opened by protocol amendment. • Part 3 will further explore GSK3145095 combined with pembrolizumab in one or more expansion cohorts. Selection of the dose of GSK3145095 and tumor types to be explored in Parts 3 will be guided by data generated in Parts 1 & 2. Part 3 will be opened by protocol amendment. • Following an amendment, Part 4 will involve dose expansion cohort(s) of GSK3145095 administered with additional anticancer agent combinations. The dose and indication will be determined based on data from Parts 1 & 2.
Time & Events	• Refer to Appendix 2: Schedule of Activities
Treatment Assignment	• This is a FTIH, open-label, non-randomized study.
Interim Analysis	• No formal interim analyses will be performed using the data generated from dose escalation cohorts (parts 1 & 2). However, data may be summarized at the completion of part 1 to determine the RP2D of GSK3145095 for part 2 and at the completion of part 2 to determine the RP2D of GSK3145095+pembrolizumab for part 3. • For Parts 3 & 4 cohort expansions, the predictive probability design by Lee and Liu will be used to assess futility. The details will be determined once the base and target response rates are specified (through an amendment). These rates will depend on the tumor-type and for part 4, the anti-cancer agent used in the combination therapy Approximately 80 participants will be enrolled in each part (3 & 4).

Note:

Due to the early study termination, Parts 2, 3 and 4 were not implemented. As a result, the remainder of this document contains no content related to Parts 2, 3 and 4, and will only provide information related to Part 1.

2.4. Statistical Hypotheses

Part 1 Dose Escalation

Due to limited enrolment in part 1, analyses for this part will be restricted to a descriptive summary of the study population and primary and secondary endpoints.

3. PLANNED ANALYSES

3.1. Interim Analyses

No interim analyses were conducted as study was terminated early during Part 1.

3.2. Final Analyses

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

1. All participants at the time of termination of study have completed the study as defined in the protocol (see protocol Section 5.3).
2. All required database cleaning activities have been completed and final database release (DBR) and database freeze (DBF) has been declared by Data Management.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses
Screened	• All participants screened for eligibility for trial entry	• Study population
All Treated	• All participants who receive at least 1 dose of GSK3145095.	• Clinical Activity • Safety • Study Population
PK	• The PK Population will consist of all participants from the All-Treated Population for whom a PK sample is obtained and analyzed.	• PK

4.1. Protocol Deviations

Major protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarised and listed as described in 11.10.4.

Protocol deviations will be tracked by the study team throughout the conduct of the study with the Protocol Deviation Specifications developed by PAREXEL.

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

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

There is no Per-Protocol Population for this study. Protocol deviations will not be used to determine membership in any study population for this study.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment

Treatment Group Descriptions			
Overall		**Data Displays for Reporting**	
Code	**General description**	**Description**	**Order in TLF**
Part 1	50 mg BID GSK3145095	50 mg BID GSK3145095	1

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. For laboratory data, baseline will be the latest non-missing pre-dose value from central lab. If no central lab value is available, the latest non-missing pre-dose value from local lab will be used. If there are multiple assessments on the same day, the mean will be used as the baseline value.

Unless otherwise stated, 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.

In general, the derived baseline values (e.g. disease assessments, vital signs, ECOG, physical examination, mean 12-lead ECG (from triplicate measurements), laboratory assessments) in summary tables and displays is the last available value prior to treatment.

5.3. Multicentre Studies

Due to early termination of the study, subject accrual will be spread thinly across centres and summaries of data by centre would be unlikely to be informative and will not, therefore, be provided.

5.4. 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
11.3	Appendix 3: Assessment Windows
11.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
11.5	Appendix 5: Data Display Standards & Handling Conventions
11.6	Appendix 6: Derived and Transformed Data
11.7	Appendix 7: Reporting Standards for Missing Data

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the All Treated Subjects population, unless otherwise specified.

Summaries of participants' disposition, protocol deviations, demographic and baseline characteristics, exposure will be based on GSK Core and Oncology Data Standards. Details of the planned displays are presented in Appendix 10: List of Data Displays.

7. EFFICACY ANALYSES

The All Treated Population will be used for anticancer efficacy analyses. Since only Part 1 was treated, the efficacy analysis is part of the secondary objective and the endpoint is Best Overall Response (BOR) based on RECIST 1.1 criteria.

7.1. Primary Efficacy Analyses

There are no primary efficacy endpoints or analyses.

7.2. Secondary Efficacy Analysis

7.2.1. Endpoint/Variables

The Part 1 efficacy analysis is based on Best Overall Response (BOR). This is defined as the best unconfirmed response (Complete Response [CR] > Partial Response [PR] > Stable Disease [SD] [or non-CR/non-PD] > Progressive Disease [PD] > Not Evaluable [NE]) from treatment start date until disease progression or initiation of new anti-cancer therapy, whichever is earlier, as assessed by the investigator per RECIST 1.1 Criteria. The BOR rate is defined as the percentage of participants with each best unconfirmed response category (CR, PR, SD, PD, or NE).

7.2.2. Summary Measure

The summary measures for the endpoints for the secondary analyses are provided in the table below.

Table 2 Summary of Summary Measures for Secondary Efficacy Analysis

Endpoint	Summary Measure
Best Overall Response (BOR) Rate (Part 1)	The number and percentage of participants with the BOR in the following response categories will be summarized: CR, PR, SD, PD and NE. Participants with unknown or missing responses will be treated as non-responders, i.e., these participants will be included in the denominator when calculating percentages of response.

8. SAFETY ANALYSES

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

All details of the planned displays are provided in Appendix 10: List of Data Displays. Unless otherwise specified, endpoints / variables will be summarised using descriptive statistics and listed.

8.1. Adverse Events Analyses

Reporting of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in full study RAP. Details on treatment emergent AEs are provided in Section 11.4.1.3 Dose Limiting Toxicity (DLT) [for GSK3145095 alone] will be and listed according to GSK Oncology Data Standards. The details of the planned displays are provided in Appendix 10: List of Data Displays.

AEs will be coded to the preferred term (PT) level using the Medical Dictionary for Regulatory Affairs (MedDRA) V22.0.AEs will be graded by the investigator according to the NCI-CTCAE (version 5.0).

A summary of non-serious AEs that occurred in strictly 20% of the participants or above will be provided (no rounding for the percentage will be used in terms of 20% threshold, e.g. events with 19.9% incidence rate should not be included in this table).

A summary of number and percentage of participants with any adverse event by maximum grade will be produced. AEs will be sorted by PT in descending order of total incidence. The summary will use the following algorithms for counting the participant:

- **Preferred term row**: Participants experiencing the same AE preferred term several times with different grades will only be counted once with the maximum grade.
- **Any event row**: Each participant with at least one adverse event will be counted only once at the maximum grade no matter how many events they have.

All AEs will be listed. Additionally, a listing of subject IDs for each individual AE will be produced.

AEs with missing date of onset will be considered treatment-emergent.

8.1.1. Deaths and Serious Adverse Events

A supportive listing will be generated to provide participant-specific details on participants who died.

A study treatment-related SAE is defined as an SAE for which the investigator classifies the relationship to study treatment as “Yes”. A worst-case scenario approach will be taken to handle missing data, i.e. the summary table will include events with the relationship to study treatment as ‘Yes’ or missing.

SAEs are included in the listing of all adverse events. Separate supportive listings with participant-level details will be generated for

- Fatal SAEs
- Non-Fatal SAEs.

8.1.2. Dose Limiting Toxicity

A listing of adverse events recorded as dose-limiting toxicities will be provided.

8.2. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Hematology laboratory tests, Urinalysis, and liver function tests will be based on GSK Core Data Standards.

The assessment of laboratory toxicities will examine the following laboratory tests performed by local laboratories:

Table 3 Clinical Laboratory Assessments

Laboratory Assessments	Parameters
Hematology	Platelet Count RBC Count Hemoglobin Hematocrit *RBC Indices*: MCV MCH *WBC count with Differential:* Neutrophils Lymphocytes Monocytes Eosinophils Basophils
Clinical Chemistry[a]	BUN, Creatinine, Glucose, Potassium, Sodium, Calcium, AST (SGOT), ALT (SGPT), Alkaline phosphatase, Total and direct bilirubin, Total Protein, Albumin32, Chloride Calculated creatinine clearance (CrCl) Carbon Dioxide
Thyroid function	Thyroid stimulating hormone, free T4, free T3
Routine Urinalysis	Specific gravity pH, glucose, protein, blood and ketones by dipstick Microscopic examination (if blood or protein is abnormal)
Other Screening Tests	Hepatitis B (HBsAg) Hepatitis C (Hep C antibody) Serum or urine β-hCG Pregnancy test (as needed for women of child bearing potential)

a. Details of liver chemistry stopping criteria and required actions and follow-up assessments after liver stopping or monitoring event are given in Protocol Section 8.1.1.

RBC = red blood cells; WBC = white blood cells; MCV = mean corpuscular volume; MCH = mean corpuscular hemoglobin; BUN = blood urea nitrogen; AST = aspartate aminotransferase; ALT = alanine aminotransferase; HBsAg = Hepatitis B surface antigen; β-hCG = beta-human chorionic gonadotropin.

Laboratory grades will be reported using the Common Terminology Criteria for Adverse Events (CTCAE v5.0).

The summary of lab values and change from baseline are required for late phase studies.The summary of lab data by max grade is normally only used for the early phase studies and there is an exemption for early phase studies to not produce the summary of lab values and change from baseline when this summary is produced.

Separate summary tables for change from baseline in grade for haematology and chemistry laboratory tests will be produced.

A listing for participants with any values of potential clinical importance for all laboratory data and urinalysis data will be produced separately.

Unless otherwise specified, the denominator in percentage calculation at each scheduled visit will be based on the number of participants with non-missing value at each visit.

8.3. Other Safety Assessments

The analyses of non-laboratory safety test results including ECGs and vital signs will be based on GSK Core Data Standards, unless otherwise specified. Performance status will be summarized and listed based on GSK Oncology Data Standard. The details of the planned displays are presented in Appendix 10: List of Data Displays.

8.3.1. Pregnancies

Any pregnancy complication or elective termination of a pregnancy for medical reasons will be recorded as an AE or SAE as described in the protocol. If the participant or participant's partner become pregnant while on the study, the information will be included in the narratives and no separate table or listing will be produced.

8.3.2. Physical Examinations and Performance Status Evaluations

A listing for Eastern Cooperative Oncology Group (ECOG) performance status will be produced.

8.3.3. Vital Signs

Change in vital signs from baseline will be summarized by scheduled visit using mean, median, standard deviation, minimum and maximum. The vital signs measurements of interest include temperature, systolic and diastolic blood pressure, and pulse rate.

8.3.4. Electrocardiograms

A summary of maximum QTc values post-baseline relative to baseline by category will be displayed. ECG values are collected in triplicates as per protocol Section 7.4.6. Average of these triplicate values will be used for all ECG reporting. Listing of ECG for participants with any value of potential clinical importance values will be produced.

8.3.5. Liver Events

The number of events does not support a summary, so only listings will be produced for medical conditions for participants with liver events.

9. PHARMACOKINETIC ANALYSES

9.1. Primary Pharmacokinetic Analyses

There are no primary PK endpoints or analyses. All PK analyses are secondary or exploratory.

9.2. Secondary Pharmacokinetic Analyses

9.2.1. Endpoint / Variables

9.2.1.1. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions. Plasma drug concentrations will be listed. descriptively summarised and plotted over time for individual subjects.

(Section 11.5.3 Reporting Standards for Pharmacokinetic)

9.2.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters for GSK3145095 alone for only Part 1 will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin.

Analysis procedures will follow GSK GUI_51487 (Version 5.0) unless otherwise noted below. All calculations of non-compartmental parameters will be based on actual sampling times.

The parameters listed in Table 4 will be calculated (if data permit) for GSK3145095.

Table 4 Summary of PK parameters calculated for GSK3145095

Parameter	Parameter Description
AUC (0-∞)	Area under the concentration-time curve extrapolated to infinity will be calculated as: AUC = AUC(0-t) + C(t) / lambda_z
AUC(0-t)	Area under the concentration-time curve from time 0 to the time of last quantifiable concentration will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC (0-τ)	Area under the concentration-time curve over the dosing interval, calculated from time zero (predose) to predose of the next dose.
C_{max}	Maximum observed plasma concentration determined directly from the concentration-time data.
T_{max}	Time to C_{max}.
$t_{1/2}$	Apparent terminal phase half-life (single dose)
C_{min}	Minimum observed plasma concentration.
Clearance	Apparent oral clearance of parent drug.

Parameter	Parameter Description
(CL/F)	
Volume of distribution (V/F)	Apparent Volume of distribution.

9.2.2. Summary Measure

- Part 1 for GSK3145095:
    - AUC (0-∞), AUC (0-t), AUC (0-τ), Cmax, Cmin, tmax, CL/F, V/F, t1/2

9.2.3. Population of Interest

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

9.2.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 10: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 9.2.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed. Analysis procedures will follow GSK GUI_51487 (Version 5.0) and GSK PK Display Standards unless otherwise noted.

GSK3145095 plasma concentration-time data will be listed by study part, dose level, study day, and nominal time, and will be summarized using descriptive statistics (n, mean, standard deviation, median, minimum, and maximum) if n for that level of summarization is ≥ 3 (if n = 2 only minimum and maximum will be reported; if n = 1 only n will be reported). Individual plasma concentration-time figure will be produced.

GSK3145095 plasma PK parameters will be listed by study part, dose level, and study day and will be summarized using descriptive statistics (n, mean, standard deviation, median, minimum, maximum, geometric mean, and geometric CV%) if n for that level of summarization is ≥ 3 (if n = 2 only minimum and maximum will be reported; if n = 1 only n will be reported).

10. REFERENCES

GlaxoSmithKline Document Number 2017N343207_03 Study ID 205013: A Phase I/II, Open-Label Study to Investigate the Safety, Clinical Activity, Pharmacokinetics, and Pharmacodynamics of GSK3145095 Administered Alone and in Combination with Anticancer Agents Including Pembrolizumab in Adult Participants with Selected Advanced Solid Tumors. 25-OCT-2018.

Ji Y, Wang SJ. Modified toxicity probability interval design: A safer and more reliable method than the 3 + 3 design for practical phase I trials. J Clin Oncol. 2013;31:1785-1791.

Neuenschwander B, Branson M, Gsponer T. Critical aspects of the Bayesian approach to phase I cancer trials. Stats Med. 2008;27:2420-2439.

11. APPENDICES

11.1. Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population

11.1.1. Exclusions from Per Protocol Population

There are no planned exclusions from the per protocol population in this study.

11.2. Appendix 2: Schedule of Activities

11.2.1. Protocol Defined Schedule of Events

Refer to Protocol Amendment 3 (2017N343207_03) Section 2, Schedule of Activities (SOA) for detailed schedule of activities for each part.

11.3. Appendix 3: Assessment Windows

11.3.1. Definition of Assessment Windows for Analyses

The visit assigned to the assessment as entered in the CRF (nominal visit) will be used for reporting.

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

11.4.1. Study Phases

Study Phase	Definition
Part 1	Dose Escalation: GSK3145095 monotherapy

11.4.1.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is before 28 days prior to earliest screening visit
Concomitant	If the medication is not Prior.

NOTES:

- Please refer to Appendix 7: 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 missing.

11.4.1.2. Study Phases for [Vital signs, ECG and Laboratory Values]

Study Phase	Definition
Pre-Treatment	Date ≤ Study Treatment Start Date
On-Treatment	Study Treatment Start Date < Date

11.4.1.3. Treatment Emergent Flag for Adverse Events

Flag	Definition

Treatment Emergent	In general, all AEs with a start date after treatment are considered emergent regardless of AE start date is before or after treatment stop date.
	• If AE onset date is on or after treatment start date & on or before treatment stop date + lag time on or before treatment stop date. (plus washout or protocol-specified time limit (e.g. half-life of drug, certain number of days, etc.).]
	  ○ Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date [+ Lag Time].
	  ○ AE Start Date is missing
	• For studies with greater than one treatment period, if AE onset is during one period and worsens during a later period it would be counted in both periods. For the initial period the logic would be as above. For the later period the logic would use the treatment dates associated with the later period:
	  ○ Treatment Period Start Date ≤ AE Worsening Date ≤ Study Treatment Stop Date [+ Lag Time].
	• Missing AE Start Date will be imputed following rules in Section 11.7.2.1 for determining Treatment Emergent AEs.

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 time of AEs should be considered, if collected.
- Lag time = 90 days if not additional anticancer agent started; 30 days if another anticancer agent is started within 90 days

11.5. Appendix 5: Data Display Standards & Handling Conventions

11.5.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: US1SALX00259
HARP Compound	: Compound: GSK3145095, study: 205013, reporting effort: final_01
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	
• RTF files will be generated for SAC.	

11.5.2. 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 participant level listings in the main body of the GSK Clinical Study Report. All participant level listings should be located in the modular appendices as ICH or non-ICH listings
• All data displays (Tables, Figures & Listings) will use the term “Subject” which reflects CDISC and GSK Data Display Standards terminology

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

• Reporting for tables, figures and formal statistical analyses:
  o Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  o 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:
  o Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1).
  o 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 IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.	

11.5.3. Reporting Standards for Pharmacokinetic Parameters

Pharmacokinetic Concentration Data	
PC Windows Non-Linear (WNL) File	PC WNL file (CSV format) for the non-compartmental analysis by Clinical Pharmacology Modelling and Simulation function will be created according to [Insert document name]. Note: Concentration values will be imputed as per GUI_51487
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.
Pharmacokinetic Parameter Data	
Is NQ impacted PK Parameters Rule Being Followed	Yes, refer to [Standards for Handling NQ Impacted PK Parameters].
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Refer to GUI_51487

11.6. Appendix 6: Derived and Transformed Data

11.6.1. 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. • 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 First Dose Date: o Ref Date = Missing → Study Day = Missing o Ref Date < First Dose Date → Study Day = Ref Date – First Dose Date o Ref Date ≥ First Dose Date → Study Day = Ref Date – (First Dose Date) + 1
Change from Baseline
• Change from Baseline = Post-Baseline Visit Value – Baseline • If either the Baseline or Post-Baseline Visit Value is missing, Change from Baseline and % Change from Baseline is set to missing
Date of Response
• For post-baseline disease assessments, the date of response (PR or better) is assigned to the latest date of disease assessments; for other response categories ([MR,] SD [or Non-CR/Non-PD], NE, PD), the date of response is assigned to the earliest date of disease assessments.

11.6.2. Study Population

Treatment Compliance
For oral drugs only • Treatment compliance will be calculated based on the formula: **Treatment Compliance = Number of Actual Doses / (Planned Treatment Duration in Days * Frequency)** • Frequency is 2 for BID and 1 for QD. Treatment compliance could be greater than 100% if there are events of overdose. Cumulative compliance (since Day 1) at each visit will be calculated.
Extent of Exposure
• Missing treatment stop date will be imputed following rules specified in Section 11.7.2.1. • Daily Oral Drugs o Number of days of exposure (duration on study treatment) to study drug will be calculated based on the formula: **Duration of Exposure in Days = Treatment Stop Date – Treatment Start Date + 1** o Participants who were randomized but did not report a treatment start date will be categorised as having zero days of exposure. o The cumulative dose will be based on the formula: **Cumulative Dose = Sum of (Number of Days x Total Daily Dose)** o If there are any treatment breaks during the study, exposure data will be adjusted accordingly.
Actual Treatment
• Participant's actual treatment will be derived from exposure data and/or study treatment data provided by Clinical Operations. If a participant's actual treatment is the same as assigned treatment, actual treatment is the assigned treatment; if a participant received treatment different from assigned treatment for the entire duration of treatment, actual treatment is different from assigned treatment.
Time since Initial Diagnosis
To report in months, divide the number of days by 30.4375; to report in weeks divide the number of days by 7; to report in years divide the number of days by 365.25. • Calculated as the number of Days from the Date of Initial Diagnosis: o First Dose Date = Missing → Elapse Time = Missing o Date of Initial Diagnosis = Completely/partially Missing → Elapse Time = Missing o Otherwise → Elapse Time = First Dose Date – Date of Initial Diagnosis + 1

11.6.3. Efficacy

Efficacy Endpoints
Best Overall Response (BOR) is defined as the best unconfirmed response (Complete Response [CR] > Partial Response [PR] > Stable Disease [SD] [or non-CR/non-PD] > Progressive Disease [PD] > Not Evaluable [NE]) from treatment start date until disease progression or initiation of new anti-cancer therapy, whichever is earlier, as assessed by the investigator per RECIST 1.1 Criteria. The BOR rate is defined as the percentage of participants with each best unconfirmed response category

11.7. Appendix 7: Reporting Standards for Missing Data

11.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion (i.e. as specified in the protocol) was defined as follows - For Part 1, participants were considered to have completed the study if they complete screening assessments and receive at least 1 study treatment and experience a DLT or completed the 4-week DLT observation period, and the treatment discontinuation visit (TDV). • A participant will be considered to have withdrawn from the study if (1) the participant has not died and is lost to follow-up, (2) the participant has withdrawn consent, (3) at the investigator's discretion is no longer being followed, or (4) the study is closed/terminated. • Withdrawn participants who discontinue before completing the 4-week DLT observation period and did not receive at least 80% of GSK3145095 (all participants) may be replaced in the study. • All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified. • Withdrawal visits will be summarised as withdrawal visits.

11.7.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: o These data will be indicated by the use of a "blank" in participant listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. o 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.

11.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays. However, where necessary, display macros may impute dates as temporary variables for sorting data in listings only. In addition, partial dates may be imputed for 'slotting' data to study phases or for specific analysis purposes as outlined below. • Imputed partial dates will not be used to derive study day, duration (e.g., duration of adverse events), or elapsed time variables (e.g., time since diagnosis). In addition, imputed dates are not used for deriving the last contact date in overall survival analysis dataset. • With the exception of new anti-cancer therapy start date in the time to event analysis dataset and exposure end date in the exposure analysis dataset, imputed dates will not be stored on datasets.

Element	Reporting Detail
Adverse Events	• Imputations in the adverse events dataset are used for slotting events to the appropriate study time periods and for sorting in data listings. • The eCRF allows for the possibility of partial dates (e.g., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: o 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. o Missing Start Month and Day: First of January will be used unless AE stop date is after treatment start date, in this case treatment start date will be used • Completely missing start dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing. • Completely or partially missing end dates will remain missing, with no imputation applied. Consequently, duration of such events will be missing.
Concomitant Medications/ Blood Supportive Products	• Completely missing start dates will not be imputed • Partial start dates for any concomitant medications recorded in the CRF will be imputed using the following convention: o If day and month are missing: – If treatment start date is missing (i.e., participant did not start study treatment), a '01' will be used for the day and 'Jan' will be used for the month; – If treatment start date is not missing ▪ If year of start date = year of study treatment start date · If stop date contains a full date which is earlier than the treatment start date, a '01' will be used for the day and 'Jan' will be used for the month; · else study treatment start date will be used ▪ else a '01' will be used for the day and 'Jan' will be used for the month o If day is missing: – If treatment start date is missing (i.e., participant did not start study treatment), a '01' will be used for the day; – If treatment start date is not missing ▪ If year and month of start date = year and month of study treatment start date · If stop date contains a full date which is earlier than the treatment start date, a '01' will be used for the day; · else study treatment start date will be used ▪ else a '01' will be used for the day and 'Jan' will be used for the month • Completely missing end dates will not be imputed • Partial end dates for any concomitant medications recorded in the CRF will be imputed using the following convention: o If day and month are missing – Earliest of (Dec 31st, date of last contact) will be used o If day is missing – Earliest of (last day of the month, date of last contact) will be used

Element	Reporting Detail

New Anti-Cancer Therapy/ Radiotherapy/ Surgical Procedures for Efficacy Evaluation (e.g., response rate, time to event)	Start dates for follow-up anti-cancer therapy, radiotherapy (where applicable), and surgical procedures (where applicable) will be imputed in order to define event and censoring rules for progression-free survival, response rate, or duration of response (i.e. start date for new anti-cancer therapy). Dates will only be imputed when a month and year are available but the day is missing. The following rules will be used to impute the date when partial start dates are present on anti-cancer therapy, radiotherapy, and/or surgical procedures dataset[s]:
	• Completely missing start dates will remain missing, with no imputation applied;
	• Partial start dates will be imputed using the following convention:
	  • If both month and day are missing, no imputation will be applied;
	  • If only day is missing:
	  ○ If the month of partial date is the same as the month of last dosing date, minimum of (last dosing date + 1, last day of the month) will be used for the day;
	  ○ If the month of partial date is the same as the month of last disease assessment and the last disease assessment is PD, minimum of (last date of disease assessment + 1, last day of the month) will be used for the day;
	  ○ If both conditions above are met, the later date will be used for the day;
	  ○ Otherwise, a '01' will be used for the day;
	• Completely or partial missing end dates will remain missing, with no imputation applied;

Treatment end date	• In general, completely missing end dates are not imputed • The imputed treatment end date will be used to calculate cumulative dose and duration of treatment as specified in Section 11.6.2 . For non-continual treatment • If treatment end date is missing for a cycle, treatment start date for the cycle will be used.

11.8. Appendix 8: Values of Potential Clinical Importance

To identify values of potential clinical importance, National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE v [5.0]) will be used to assign grades for laboratory parameters including clinical chemistry, hematology, liver function tests.

The clinical importance for vital signs (temperature and blood pressure) are also identified using NCI-CTCAE v [5.0] with details below. Pulse rate below 60 beats/min is indicated as low and above 100 beats/min is indicated as high.

	Grade 0	Grade 1	Grade 2	Grade 3
Temperature	<38	38-39	>39-40	>40
Systolic Blood Pressure	<120	120-139	140-159	>=160
Diastolic Blood Pressure	<80	80-89	90-99	>=100

Reference ranges for all laboratory parameters collected throughout the study are provided by the laboratory. A laboratory value that is outside the reference range is considered either high abnormal (value above the upper limit of the reference range) or low abnormal (value below the lower limit of the reference range). Note: a high abnormal or low abnormal laboratory value is not necessarily of clinical concern. The laboratory reference ranges will be provided on the listings of laboratory data. Clinical laboratory test results outside of the reference range will be flagged in the listings.

11.9. Appendix 9: Abbreviations & Trade Marks

11.9.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
A&R	Analysis and Reporting
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
CSR	Clinical Study Report
CTR	Clinical Trial Register
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
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
IMMS	International Modules Management System
ITT	Intent-To-Treat
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PK	Pharmacokinetic
PP	Per Protocol
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
SDSP	Study Data Standardization Plan
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
TFL	Tables, Figures & Listings

11.9.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS

11.10. Appendix 10: List of Data Displays

Please note that in all tables, listings, and figures, the term "subject(s)" is used to refer to "participants".

11.10.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.6	N/A
Efficacy	2.1	N/A
Safety	3.1 to 3.6	N/A
Pharmacokinetic	4.1 to 4.2	4.1
Section	**Listings**	
ICH Listings	1 to 25	
Other Listings	26 to 34	

11.10.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Section 11.10: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln

NOTES:

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

11.10.3. Deliverables

Delivery	Description
SAC	Final Statistical Analysis Complete

11.10.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.1	All Treated Subjects	ES1	Summary of Subject Status and Reason for Study Withdrawal – Part 1	ICH E3, FDAAA, EudraCT	SAC
1.2	Enrolled	NS1	Summary of Number of Participant by Country and Site ID– Part 1	EudraCT/Clinical Operations	SAC
Demographic and Baseline Characteristics					
1.3	All Treated Subjects	DM1	Summary of Demographic Characteristics– Part 1	ICH E3, FDAAA, EudraCT	SAC
1.4	All Treated Subjects	DM5	Summary of Race and Racial Combinations– Part 1	ICH E3, FDA, FDAAA, EudraCT	SAC
Exposure and Treatment Compliance					
1.5	All Treated Subjects	POP_T1	Summary of Exposure to GSK3145095– Part 1		SAC
Protocol Deviation					
1.6	All Treated	DV1	Summary of Important Protocol Deviations – Part 1	ICH E3	SAC

11.10.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Clinical Response					
2.1	All Treated	RE1a	Summary of Investigator-Assessed Best Response without Confirmation for Subjects with Measurable Disease only at Baseline (RECIST 1.1 Criteria)	1. Include just the first two segments of the template. i.e. Best Response and Response rate. 2. P-value for response rate would not be reported.	SAC

11.10.6. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Adverse Events (AEs)					
3.1	All Treated	OAE7	Summary of All Adverse Events by Maximum Grade by Preferred Term	Use AE1 or AE1CP if Grade/Intensity not used; otherwise use AE5A/B (with a Total column across all grades/severities, which provides same detail as AE1.)	SAC
3.2	All Treated	AE15	Summary of Common (>=20%) Non-serious Adverse Events by Preferred Term (Number of Participant and Occurrences)	FDAAA, EudraCT	SAC
Laboratory: Chemistry					
3.3	All Treated	OLB11C	Summary of Clinical Chemistry Changes from Baseline with Respect to The Normal Range	.	SAC
Laboratory: Hematology					
3.4	All Treated	OLB11C	Summary of Haematology Changes from Baseline with Respect to The Normal Range		SAC
ECG					
3.5	All Treated	OECG1C	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category– Part 1	IDSL	SAC
Vital Signs					
3.6	All Treated	VS1	Summary of Change from Baseline in Vital Signs – Part1	ICH E3	SAC

11.10.7. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
PK Concentration					
4.1	PK	PK01	Summary of GSK3145095 Plasma Pharmacokinetic Concentration-Time Data	IDSL	SAC
PK Parameters					
4.2	PK	PK06	Summary of Derived GSK3145095 Plasma Pharmacokinetic Parameters (non-transformed and log-transformed)	IDSL	SAC

11.10.8. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK					
4.1	PK	PK16a/b	Individual GSK3145095 Plasma Concentration-Time Plots (Linear and Semi-log)	IDSL Required for serial sampling but not sparse sampling. Required for late-phase if PK data being analyzed by S&P and serial sampling was done.	SAC

11.10.9. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.	Screened	ES7	Listing of Reasons for Screen Failure	Journal Guidelines	SAC
2.	All Treated	ES2	Listing of Reasons for Study Withdrawal		SAC
3.	All Treated	SD2	Listing of Reasons for Study Treatment Discontinuation	Remove “Number of cycles” column. Add investigational product as one of the column	SAC
Protocol Deviations					
4.	All Treated	DV2	Listing of Important Protocol Deviations		SAC
5.	Screened	IE3	Listing of Participants with Inclusion/Exclusion Criteria Deviations		SAC
Populations Analysed					
6.	All Treated	SP3	Listing of Participants Excluded from Any Population	e.g., participants screened but not randomized, participants randomized but not treated, participants with deviations leading to exclusion from per protocol population (can be separate listing per population).	SAC

Demographic and Baseline Characteristics					
7.	All Treated	DM2	Listing of Demographic Characteristics		SAC
8.	All Treated	DM9	Listing of Race		SAC
Medical History and Concomitant Medications					
9.	All Treated	MH2	Listing of Past/Current Medical Conditions	Oncology specific template to be used	SAC
10.	All Treated	OCM1A	Listing of Concomitant Medications	Include both prior and concomitant medications	SAC
Exposure and Treatment Compliance					
11.	All Treated	EX3	Listing of Exposure Data	Include a flag variable to indicate imputed date.	SAC
12.	All Treated	COMP2	Listing of Overall Compliance		SAC
Adverse Events					
13.	All Treated	OAE04	Listing of All Adverse Events	ICH E3	SAC
14.	All Treated	OAE03	Listing of Subject Numbers for Individual Adverse Events	ICH E3	SAC
Serious and Other Significant Adverse Events					
15.	All Treated	OAE04	Listing of Fatal Serious Adverse Events		SAC
16.	All Treated	OAE04	Listing of Non-Fatal Serious Adverse Events		SAC
17.	All Treated	AE8 / AECP8 / AE9 / AE9CP	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	SAC
Dose-Limiting Toxicities					
18.	All Treated	DL3	Listing of Dose-Limiting Toxicities (DLT) During the Determinative Period	Required for dose escalation studies looking at dose-limiting toxicities.	SAC

All Laboratory					
19.	All Treated	LB5A	Listing of All Laboratory Data	ICH E3 May be split into separate listings by chemistry, hematology, etc. Display ALL labs for a subject who experienced a value of potential clinical importance. Recommended for oncology: LB5A; For healthy volunteer studies, LB5/6 is recommended.	SAC
ECG					
20.	All Treated	EG3	Listing of All ECG Values for Participants with Any Value of Potential Clinical Importance	IDSL Required for ClinPharm studies only. Display ALL ECGs for a subject who experienced a value of potential clinical importance.	SAC
Vital Signs					
21.	All Treated	VS4	Listing of Vital Signs		SAC
Deaths					
22.	All Treated	DTH3	Listing of Deaths	ICH E3	SAC
Hepatobiliary (Liver)					
23.	All Treated	MH2	Listing of Medical Conditions for Participants with Liver Stopping Events	IDSL	SAC
Performance Status					
24.	All Treated	PS5A	Listing of Performance Status	Example PS5A is used to list ECOG Performance Status.	SAC

11.10.10. Non-ICH Listing

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Disease Characteristics					
25.	All Treated	DC3	Listing of Disease Characteristics at Initial Diagnosis		SAC
26.	All Treated	DC4	Listing of Disease Characteristics at Screening		SAC
27.	All Treated	MD2	Listing of Metastatic Disease at Screening	Include if this information is collected in the eCRF. Will not be appropriate for heme studies.	SAC
Anti-Cancer Therapy					
28.	All Treated	AC6	Listing of Prior Anti-Cancer Therapy		SAC
29.	All Treated	AC7	Listing of Prior Anti-Cancer Radiotherapy		SAC
Surgical Procedures					
30.	All Treated	OSP3	Listing of Prior Treatment Cancer Related Surgical Procedures		SAC
Substance Use					
31.	All Treated	SU2	Listing of Substance Use		SAC
Responses					
32.	All Treated	LA5	Listing of Investigator Assessed Lesion Assessments (RECIST v1.1 Criteria) -Part 1		SAC [1]
PK					
33.	PK	PK07	Listing of GSK3145095 Plasma Pharmacokinetic Concentration-Time Data	IDSL	SAC
34.	PK	PK13	Listing of Derived GSK3145095 Plasma Pharmacokinetic Parameters	IDSL	SAC

11.11. Appendix 11: Example Mock Shells for Data Displays

Example: POP_T1 Page 1 of n

Protocol: 205013

Population: All Treated Subjects

Table X
Summary of Exposure to GSK3145095

		50 mg BID
Duration of Exposure(weeks) [1]	n	X
	Mean	X.XXX
	SD	X.XXXX
	Median	X.XXX
	Min.	X.XX
	Max.	X.XX
Average Daily Dose(mg) [2]	n	X
	Mean	X.XXX
	SD	X.XXXX
	Median	X.XXX
	Min.	X.XX
	Max.	X.XX

Note: [1] Duration of exposure = end date of GSK3145095- start date of GSK3145095 + 1.
[2] Average daily dose = Cumulative dose divided by duration of exposure.