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

Protocol Title	:	A Phase I First Time in Human Open Label Study of GSK3745417 administered with and without Anticancer Agents in Participants with Advanced Solid Tumors
Study Number	:	208850
Compound Number	:	GSK3745417, GSK4057190 (dostarlimab)
Effective Date	:	01 May 2024

Description:

- The purpose of this RAP is to describe the planned analyses and outputs to be included in the Clinical Study Report (CSR) based on Protocol Amendment 7, TMF-16209529. This corresponds to the final analysis.
- The RAP also covers two other types of reporting efforts: Dose Escalation Meetings (DEMs) for monotherapy and Investigator Brochure (IB) updates. Outputs for the monotherapy DEM and IB update reporting efforts, which are not required for the final analysis, are included in the RAP but are distinguished from those needed for the final analysis.

RAP Author(s):

Author
PPD Study Lead Statistician, Clinical Statistics

RAP TEAM REVIEW CONFIRMATIONS

(Method: Veeva Collaborative Author Workflow**)**

Reviewer	Date
PPD Clinical Scientist, Clinical Development	See Veeva
PPD Medical Monitor, Clinical Development	See Veeva
PPD Safety Lead, Pharma Safety	See Veeva
PPD Safety Evaluation and Risk Management (SERM) Physician, SERM	See Veeva
PPD Clinical Pharmacology Modelling & Simulation (CPMS) Lead	See Veeva
PPD Study Co-Lead Programmer, Clinical Programming	See Veeva
PPD Study Co-Lead Programmer, Clinical Programming	See Veeva
PPD Clinical Trial Transparency Statistician, Clinical Trial Transparency	See Veeva

CLINICAL STATISTICS & CLINICAL PROGRAMMING LINE APPROVALS

(Method: Veeva Approval Workflow**)**

Approver	Date
PPD Project Statistician, Clinical Statistics	See Veeva
PPD Project Programmer, Clinical Programming	See Veeva

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VERSION HISTORY

RAP Version	Approval Date	Protocol Version (Date) on which SAP is Based	Change	Rationale
1	21Feb2019	Protocol Amendment 1 (12Dec2018)	Not Applicable	Original Version
2	22Jan2020	Protocol Amendment 1 (12Dec2018)	Removal of Part 1B, Part 2A and 2B. Further detail provided for study population analyses. Removal of efficacy section. Added pharmacodynamic/biomarker analysis section. Added in list of data displays.	To focus on IB and FDA reporting efforts.
3	01Feb2024	Protocol Amendment 7 (04Aug2023)	CCI [redacted] Updated RAP according to early study closure, including reducing the list of outputs (includes removal of pharmacodynamic/biomarker analysis section). Dose escalation method changed to BLRM. Updated study design and analysis sets. Added in crossover considerations. Added in efficacy section.	CCI [redacted] Protocol amendments since previous RAP version. Introduction of RAPIDO DV to reduce the number of static listings to be produced.

			Updated RAP text and list of outputs to remove those that will be produced by RAPIDO DV. Updated the outputs required for the IB based on the streamlining of the IB (data cut off in 2023). General corrections and minor updates.	
4	See Veeva	Protocol Amendment 7 (04Aug2023)	Clarification added to the secondary endpoint. Confirmation that the study will transition to PACT (Section 3.3). General corrections, clarifications, and minor updates.	Final review prior to database lock.

The RAP versions can be found under the following files and versions in Veeva (due to the migration of the documents into Veeva during the study).

RAP Version	Approval Date	Veeva File Name	Veeva Version(s)
1	21Feb2019	Statistical Analysis Plan RAP Critical Components	1-5
2	22Jan2020	Statistical Analysis Plan RAP-Reporting and Analysis Plan for IB and FDA outputs	1-3
3	01Feb2024	Statistical Analysis Plan RAP-Reporting and Analysis Plan for IB and FDA outputs	4
4	See Veeva	Statistical Analysis Plan RAP-Reporting and Analysis Plan for IB and FDA outputs	5

1. INTRODUCTION

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

Protocol Revision Chronology:		
2017N347464_00	12-SEP-2018	Original Protocol
2017N347464_01	12-DEC-2018	Protocol Amendment 1
2017N347464_02	27-AUG-2020	Protocol Amendment 2
2017N347464_03	16-OCT-2020	Protocol Amendment 3
TMF-11921930	21-APR-2021	Protocol Amendment 4
TMF-14427782	19-JAN-2022	Protocol Amendment 6
TMF-16209529	04-AUG-2023	Protocol Amendment 7

CCI [redacted]. A synoptic CSR will be used to report the study and the RAP reflects the reduced list of outputs required for a synoptic CSR (and disclosure).

The RAP focuses on the outputs required for the final analysis, which will be included in the CSR. The RAP also covers two other types of reporting efforts: Dose Escalation Meetings (DEMs) and Investigator Brochure (IB) updates. Note that Statistics and Programming (S&P) provided the outputs for the monotherapy DEMs (Part 1A) and the Study Team provided outputs for the combination DEMs (Part 2A) using appropriate in-stream software. Outputs for the DEM and IB update reporting efforts, which are not required for the final analysis, are included in the RAP but are distinguished from those needed for the final analysis.

This study will utilize the system RAPIDO DV for the final analysis to aid with data visualization. Therefore, only listings that will be produced statically will be discussed in the RAP and included in the list of data displays in the Appendix. Where listings were produced statically for DEMs and IB updates, these will continue to be included in the RAP and will be distinguished as such.

1.1. Imaging Substudy

The analyses for the primary and secondary endpoints for the Imaging Substudy are detailed in a separate plan produced by the Amsterdam University Medical Centers (AUMC). CCI [redacted].

In summary, all applicable analyses for the Imaging Substudy are detailed in separate analysis plans, when performed. Therefore, the Imaging Substudy will not be discussed

in this RAP. Note that the participants in the Imaging Substudy will still be included in the analyses for the main study endpoints.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the current protocol (Protocol Amendment 7, dated 04 Aug 2023). However, due to the early closure of the study, some analyses or displays described in the protocol may no longer be required. Clarification has been given in the RAP on the secondary endpoint regarding PK parameters.

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

Dose Escalation (Part 1A GSK3745417 Monotherapy and Part 2A Combination GSK3745417 and Dostarlimab)	
Objectives	**Endpoints**
Primary Objectives	**Primary Endpoints**
• To determine the safety, tolerability, and the recommended phase 2 dose (RP2D) of GSK3745417 alone or in combination with dostarlimab administered intravenously to participants with advanced/recurrent solid tumors.	• Incidence of DLT. • Incidence and severity of adverse events.
Secondary Objectives	**Secondary Endpoints**
• To characterize the PK properties of GSK3745417 alone or in combination with dostarlimab.	• GSK3745417 concentrations in plasma and PK parameters including AUC(0-tau), maximum observed concentration (Cmax), and terminal half-life (t1/2), as data permit.
Exploratory Objectives	**Exploratory Endpoints**
CCI [redacted]	

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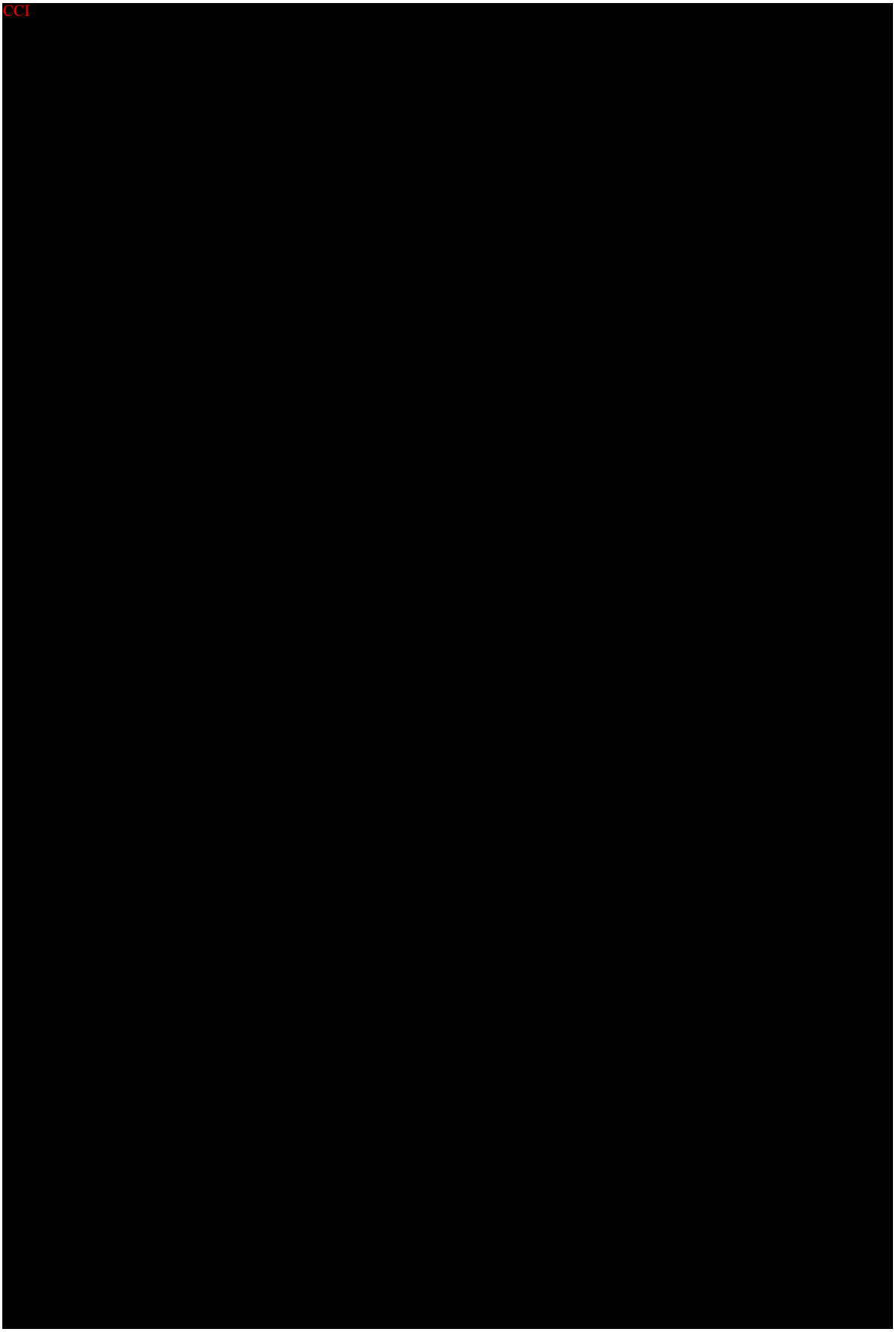

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2.3. Study Design

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Design Features	• In Part 1A, safety and tolerability of escalating doses of GSK3745417 (Q1W in Arm A1 and Q3W in Arm A2) will be evaluated according to Bayesian Logistic Regression Model (BLRM) design. o Part 1A was completed. • In Japan, a stand-alone monotherapy dose escalation will be conducted to evaluate the safety, tolerability, PK/PD and preliminary clinical activity of GSK3745417(Q1W) in a Japanese population. The safety and tolerability of escalating doses of GSK3745417 (Q1W) will be evaluated, and a 3+3 dose-escalation procedure will be utilized. o The Japan monotherapy dose escalation was prematurely stopped. • Note that upon the clearance for safety of a dose in Part 2A combination therapy dose escalation, participants in Part 1A (including the Japan monotherapy cohorts) may be considered at confirmed disease progression and on a case-to-case basis to transition to a cleared combination dose/frequency regimen as tested in Part 2A. • Once a dose of GSK3745417 has been identified that is tolerable and demonstrates potential pharmacodynamic activity (based on the totality of the data), enrolment in Part 2A may begin. Starting at a dose of 0.1 mg

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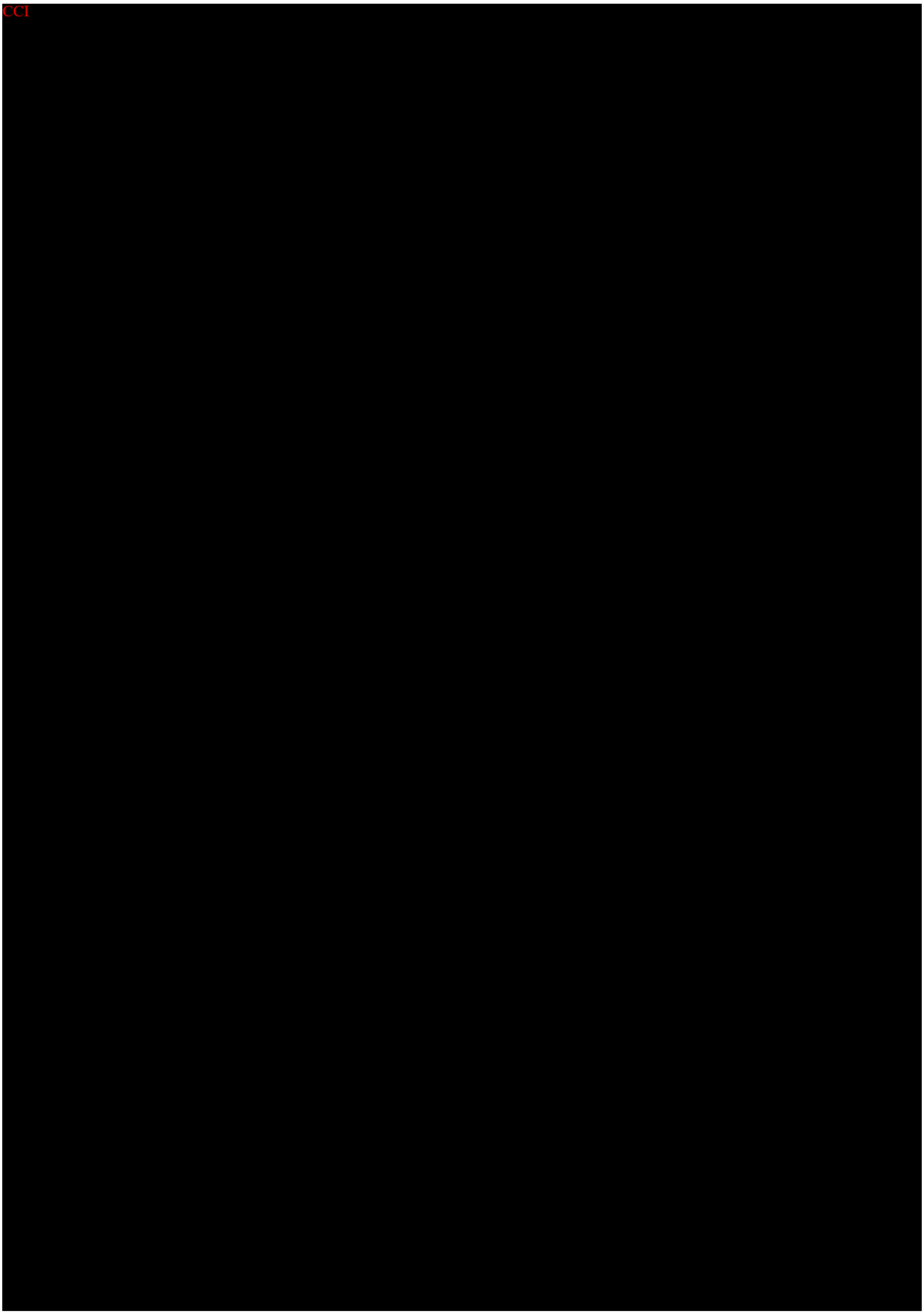

Overview of Study Design and Key Features	
	CCI [redacted]
Time & Events	• [Refer to Appendix 2: Schedule of Activities]
Treatment Assignment	• This is a first time in human, open label, repeat dose, non-randomized study. • BLRM will be used to guide the dose escalation decisions in Parts 1A and 2A. • The 3+3 dose-escalation procedure will be used to guide the dose escalation decisions in the Japan monotherapy cohort. • CCI [redacted]
Interim Analysis	• For dose escalation and de-escalation decisions, preliminary safety and available PK/Pharmacodynamic data will be analysed and reviewed by the Study Team (to include at minimum, the GSK medical monitor and investigators) after completion of each dose cohort. This review will support the decision on the dose level in the next dose cohort. • Additional interim analyses may be conducted in any part of the study to support IB/Development Safety Update Reports, publications, internal governance board meetings, and planning of future studies.

2.4. Statistical Hypotheses / Statistical Analyses

CCI [redacted]

3. PLANNED ANALYSES

3.1. Part 1A and 2A: Dose Escalation (Monotherapy and combination therapy with dostarlimab)

Dose escalation for GSK3745417 monotherapy will begin with a starting dose of 0.1 mg in both Arm A1 and Arm A2. There will be two arms in Part 1A: GSK3745417 monotherapy at every 1-week interval (Q1W) in Arm A1, and GSK3745417 monotherapy at every 3-week interval (Q3W) in Arm A2. The first 3 participants in the first 4 dose levels in each arm will begin treatment ≥48 hours apart to allow assessment of initial safety data in each participant before beginning the next participant's treatment. This staggered dosing start is not required for participants enrolling at previously cleared dose levels and may be waived once sufficient data are available. In exceptional cases, intra-participant dose escalation allowing participants to move from a lower to a higher dose not exceeding the MTD will be discussed with investigators and approved by the GSK Medical Monitor. Once a 21-day for Arm A1 or 29-day for Arm A2 DLT evaluation period has been completed, BLRM analysis will be performed to guide the dose level to which the next 3 participants will be assigned based on the posterior probability of the DLT rate.

Select outputs will be provided by S&P for monotherapy dose escalation meetings (Part 1A). These are indicated in Appendix 10 by the DEM reporting effort. The following outputs were created for DEMs only and are therefore not referred to in the main RAP text:

- A summary of the number of DLTs, adverse events (AEs) and serious adverse events (SAEs) for all DLT evaluable subjects
- A summary of the number of events and subject by maximum grade for DLT evaluable subjects
- A listing of serious adverse events for DLT evaluable subjects
- A listing of grade >= 3 laboratory data for complete blood count (CBC) with differential for DLT evaluable subjects

There will be two arms in Part 2A: combination of GSK3745417 Q1W and dostarlimab in Arm A3, and combination of GSK3745417 Q3W and dostarlimab in Arm A4. Dostarlimab will be added to this regimen starting at Week 1 of the GSK3745417 dosing schedule and administered at 500 mg dose Q3W for the first 4 doses, followed by 1000 mg Q6W for subsequent doses. The first 3 participants in each dose level will begin treatment ≥48 hours apart to allow assessment of initial safety data in each participant before beginning the next participant's treatment. Each participant must complete the 29-day DLT evaluation period and the available safety data must be reviewed before a decision is made on whether to proceed to the next dose level. Once a 29-day DLT evaluation period has been completed, BLRM analysis will be performed to guide the dose level to which the next 3 participants will be assigned based on the posterior probability of the DLT rate. If a participant withdraws from the study before completion of the 29-day DLT period for reasons other than DLT, the participant will not be counted as DLT evaluable and will be replaced.

For the combination dose escalation meetings (Part 2A), the outputs for the DEMs will be provided by the Study Team (not S&P) using appropriate, in-stream software.

3.1.1. Description of the Bayesian Logistic Regression Model (BLRM)

After each dose cohort, BLRM will be used to guide dose escalation decisions for monotherapy and combination therapy. The BLRM methodology will be implemented separately for Q1W dosing schedule and Q3W dosing schedule. At the time of each dose escalation decision, BLRM will be used to obtain, for each potential dose, an updated estimate of the toxicity curve and the posterior probabilities that the DLT rate for that dose lies in each of four toxicity intervals (underdosing, target toxicity range, excessive toxicity, and unacceptable toxicity). The four DLT toxicity intervals are defined as follows:

- [0%, 16%) Under-dosing range;
- [16%, 33%) Target toxicity range;
- [33%, 50%) Excessive toxicity range;
- [50%, 100%) Unacceptable toxicity range;

The dose with the highest posterior probability of lying in the Target Toxicity range will be the model-recommended dose for the next cohort. Additionally, the following constraints for the recommended dose will be maintained:

- The posterior probability of the DLT rate lying in the Excessive Toxicity or Unacceptable Toxicity range is less than 25%.
- The recommended dose is no more than two-fold (100%) of the previous dose.

Note that de-escalation as well as escalation is possible using this method.

Dose escalation will continue until:

i. An MTD is found:

At least 9 participants have been treated at the current target dose

AND

The posterior probability that the DLT rate for the current dose lies in either the excessive toxicity or unacceptable toxicity range is less than 25%

AND

The posterior probability that the DLT rate for the next higher dose lies in either the excessive toxicity or unacceptable toxicity range is greater than or equal to 25%.

OR

ii. The maximum administered dose has been reached and at least 9 participants have been dosed at that dose level.

OR

iii. All doses have a posterior probability of lying in either the excessive toxicity or unacceptable toxicity range of greater than or equal to 25%

AND

At least two DLTs have been observed.

3.2. Japan: Dose Escalation (Monotherapy)

CCI [redacted]

Table 1 3+3 Dose-escalation Guidelines

Number of Participants with DLT at a Given Dose Level	Action
0 of 3	Escalate to the next dose level
1 of 3	Accrue 3 additional participants at current dose level for a total of 6 evaluable participants. • If 0 of the additional 3 participants experience a DLT, escalate to next dose level. • If ≥1 of the additional 3 participants experiences a DLT, stop dose escalation.
1 of 6	Escalate to the next dose level
≥2 of up to 6	Stop dose escalation

CCI [redacted] dose escalation cohort will be analyzed separately from the monotherapy dose escalation study conducted outside CCI [redacted]

The Japan monotherapy dose escalation cohort was closed to recruitment after 2 participants had been enrolled. Therefore, no decisions were made regarding dose escalation as 3 DLT evaluable participants were not recruited.

3.3. Final Analysis

The final analysis will be performed after the completion of the following sequential steps:

1. All participants have completed the study as defined in the protocol (see Protocol Section 4.3). Under Protocol Amendment 7, participants will be considered to have completed the study if they complete the safety follow-up until 90 days after last dose, start subsequent therapy or die. As per RAP version 4, the study will transition to a Post Analysis

Continuation of Treatment (PACT) phase, in which case the implementation of PACT will trigger the final analysis.

2. All required database cleaning activities have been completed and final database release (DBR) and database freeze (DBF) has been declared by Data Management (DM).

4. ANALYSIS SETS

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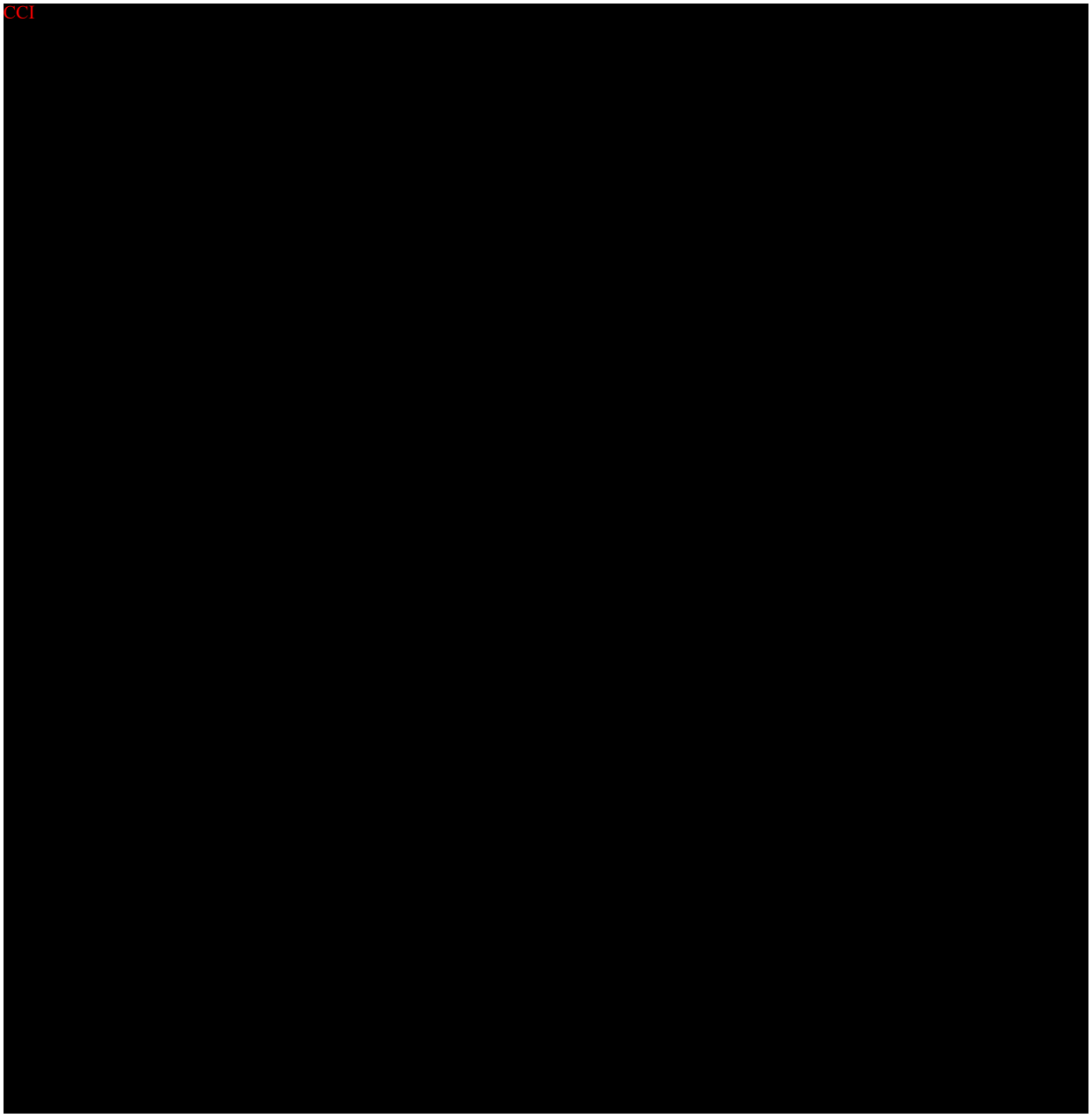

4.1. DLT Evaluable

Additional considerations are needed for determining whether participants are DLT evaluable:

- Participants must receive at least 80% of the scheduled dose in the DLT period to be DLT evaluable. This only has implications on CCI

CCI [redacted]

DLT reconciliation meeting(s) will be held to ensure all applicable participants in CCI [redacted] are correctly determined as DLT evaluable or not in the ADaM datasets and displays.

- Clinical, safety, statistics, clinical programming and clinical operations will attend as a minimum.
- S&P will create a listing of applicable participants with a derived DLT evaluable flag, which is calculated programmatically based on the criteria above.
- The clinical team will provide a listing of the same applicable participants with the DLT evaluable flag based on the DEMs and any other relevant information.
- Any differences between the clinical list and S&P list will be reviewed.
    - If possible, the S&P algorithm will be updated to match the listing provided by the clinical team.
    - If it is not possible to update the algorithm (for example, the necessary data has not been collected in the eCRFs), then the team will agree and approve the listing from clinical. The agreed listing from clinical will be deemed the final listing and will be used as the source data for the DLT evaluable flag (that is, for the analyses after the DLT reconciliation meeting(s), the DLT evaluable flag will come from the final list and will not be calculated programmatically by S&P).
- The meeting minutes will include the final DLT evaluable list. The meeting minutes will be filed in the eTMF.

5. PROTOCOL DEVIATIONS

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, participant management or participant assessment) will be summarized and listed based on the All Treated analysis set. The table and listing will include the crossover cohorts.

Protocol deviations will be tracked by the Study Team throughout the conduct of the study. These protocol deviations will be reviewed to identify those considered as important as follows:

- Data will be reviewed prior to freezing the database to ensure all important deviations are captured and categorized in the protocol deviations Study Data Tabulation Model (SDTM) dataset.

- This SDTM dataset will be the basis for the summary and listing of important protocol deviations.

The number and percentage of participants who entered the trial and had important protocol deviations defined as part of the protocol deviation management plan for the study will be summarized. The protocol deviations categories will be sorted in descending order based on total incidence, and within category, the protocol deviation coded terms will be sorted in descending order based on total incidence. A participant listing of the important protocol deviations will also be produced, including treatment, site ID, unique subject ID, subject ID, date of deviation, study day of deviation, period day of deviation, protocol deviation category, protocol deviation coded term, protocol deviation description and relationship to COVID-19. The listing will be sorted by treatment, site ID, unique subject ID, subject ID, and date of deviation.

A separate listing of all inclusion/exclusion criteria deviations will be provided based on the All Treated analysis set. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF. The listing will include site ID, treatment group, unique subject ID, subject ID, inclusion/exclusion type, protocol version and criteria description. The listing will be sorted by treatment, site ID, unique subject ID, and subject ID.

CCI [redacted]

6. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

6.1. Study Treatment & Sub-group Display Descriptors

All displays will be displayed by study part and order of treatment group as indicated below in the last column "Order in TLF". The cohorts are ordered by increasing dose intensity considering the dose and regimen.

Treatment Group Descriptions				
REGIMEN Dataset		**Data Displays for Reporting**		
Code	**Regimen Description**	**Study Part**	**Treatment Group Description**	**Order in TLF**
CCI	[redacted]			

Treatment Group Descriptions
CCI [redacted]

6.1.1. Japan Monotherapy Cohort

Data from the Japan monotherapy cohort will be included as a separate cohort. The cohort will be displayed alongside the main study cohorts in Part 1A and will be included in the Part 1A Total column.

6.1.2. Imaging Substudy Combination Cohort

Data from the Imaging Substudy cohort will be included as separate cohorts. The cohorts will be displayed alongside the main study cohorts in Part 2A and will be included in the Part 2A Total column.

6.1.3. Crossover Cohorts

As per Protocol Amendment 6, participants in Part 1A may be considered on a case-by-case basis to transition to a cleared combination dose/frequency regimen as tested in Part 2A.

For participants who cross over to Part 2A from Part 1A, the data occurring prior to crossover will be considered for analysis in the Part 1A cohorts.

For all study population, safety and PK displays, the data occurring after crossover will be included in the applicable displays. In most cases, this will be via the addition of separate crossover combination cohorts (considered the standard approach in this study). When a different approach is required to display the crossover data, details are provided. The approach will be indicated in the programming notes column in Section 12.10 and in the mock shells. For the efficacy table, data occurring after crossover are not included in the display.

The crossover cohorts are labelled according to the subsequent combination therapy dose/regimen. All possible crossover cohorts have been listed in Section 6.1, however, only the crossover cohorts with at least one participant will be included in the displays.

Japan monotherapy participants who cross over to combination therapy will be included in the main study crossover cohorts (that is, there will not be separate Japan crossover cohorts).

The date of crossover is defined as in Section 12.6.4.

6.2. 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. For crossover participants, the baseline value for data included in the crossover combination cohort will be the latest pre-combination dose 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. If there are multiple assessments on the same day, the mean will be used as the baseline value.

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

6.3. Other Considerations for Data Analyses and Data Handling Conventions

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

Section	Component
12.3	Appendix 3: Assessment Windows
12.4	Appendix 4: Study Phase and Treatment Emergent Flag for Adverse Events
12.5	Appendix 5: Data Display Standards & Handling Conventions
12.6	Appendix 6: Derived and Transformed Data
12.7	Appendix 7: Reporting Standards for Missing Data
12.8	Appendix 8: Values of Potential Clinical Importance

7. STUDY POPULATION ANALYSES

7.1. Overview of Planned Study Population Analyses

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

Study population analyses will be based on GSK Core and Oncology Data Standards. Details of the planned displays are presented in Appendix 10: List of Data Displays. Study population summary tables will include columns for treatment groups and a total column within each Part, see Section 6.1.

7.2. Disposition of Participants

A listing of participants excluded from the All Treated analysis set will be presented on the Enrolled analysis set.

The number of participants by country and site ID will be summarized using the Enrolled analysis set (and using the All Treated analysis set if different from the Enrolled analysis set).

A summary table and listing identifying reasons for screen failures will be presented based on the Screened Population. This summary will show the number and percentage of participants who entered the trial, failed and reasons for failure. The listing will include site ID, unique subject ID, subject ID, date of screening, and the reason term(s) for screen failure.

A summary of the number and percentage of participants who crossover from Part 1A (including the Japan cohorts) into each crossover combination will be produced.

A summary of participant status and reason for study withdrawal will be provided. Participants in Part 1A will be split into those who did and did not crossover to combination therapy. Participants in Part 1A who did crossover will be grouped by their crossover cohort. For those who crossed over to combination therapy, the display reflects their status regarding their combination therapy. This display will show the number and percentage of participants who have completed the study, were ongoing (as part of PACT) and have withdrawn from the study. ‘Completed’ will be sub-categorized into ‘Completed follow-up’ and ‘Died’, and 'Ongoing’ will be sub-categorized into ‘On study treatment’ and ‘In follow-up’. Reasons for study withdrawal will be presented in the order they are displayed in the eCRF. Participants are assigned to the categories and sub-categories as follows:

- ‘Completed’: Participant either ‘Completed follow-up’ or ‘Died’.
- ‘Completed follow-up’: Site indicated on the end of study eCRF that the participant did not discontinue the study before completing all follow-up.
- ‘Died’: Site indicated that the participant died on the death eCRF.
- ‘Ongoing’: Participant is either ‘On study treatment’ or ‘In follow-up’.
- ‘On study treatment’: Site indicated on the end of study eCRF that the participant discontinued due to ‘Protocol-defined stopping criteria’ and the specify field includes both the strings “PACT” and “continuing treatment”.

- 'In follow-up': Site indicated on the end of study eCRF that the participant discontinued due to 'Protocol-defined stopping criteria' and the specify field includes both the strings "PACT" and "90 day safety follow-up".
- 'Withdrawn': Site indicated on the end of study eCRF that the participant discontinued the study before completing all follow-up and the criteria for 'Ongoing' is not satisfied.

The required follow-up (and therefore definition of completer) changed in Protocol Amendment 7 **from** two years of follow-up from first dose **to** 90 days of follow-up from last dose or until start of subsequent anti-cancer therapy, whichever is first.

The study disposition table will be repeated on the Enrolled analysis set, if this differs from the All Treated analysis set.

A listing of reasons for study withdrawal will also be provided and will include treatment group, site ID, unique subject ID, subject ID, crossover, date of withdrawal, study day, period day, date of last contact, primary reason, reason specify (if collected), was a follow-up phone contact attempted 3 times, was a follow-up certified letter mailed, and relationship to COVID-19.

A summary of study treatment status and reasons for discontinuation of study treatment will be provided separately for GSK3745417 and dostarlimab. The summary of study treatment status and reasons for discontinuation of study treatment for **GSK3745417** will show the number and percentage of participants who are ongoing on study treatment (as part of PACT) or have discontinued study treatment, and primary reason for discontinuation of study. Discontinued has a sub-category of crossover to indicate how many of the participants from Part 1A entered a crossover combination cohort. The crossover cohorts will also be included in the display and will show the treatment status of the combination therapy for the crossover participants. The summary of study treatment status and reasons for discontinuation of study treatment for **dostarlimab** will show the number and percentage of participants who are ongoing on study treatment (as part of PACT) or have discontinued study treatment, and primary reason for discontinuation for all the dose levels in Part 2A, as mentioned in Section 6.1, and for the crossover cohorts. Reasons for study treatment discontinuation will be reported in the order they are displayed in the eCRF.

Reasons for discontinuation of treatment will be listed separately for GSK3745417 and dostarlimab. The listings will include treatment group, site ID, unique subject ID, subject ID, date of decision made to discontinue and study day, period day, date of last dose and study day, period day, primary reason of discontinuation of treatment, reason specify and relationship to COVID-19. Both listings will include crossover information. The listing for **GSK3745417** will also include treatment sequence (M = monotherapy only vs. MC = monotherapy then combination therapy (crossover) vs. C = combination therapy only), treatment and period (monotherapy vs. combination therapy). It will include two rows for crossover participants: one for GSK3745417 as monotherapy and one for GSK3745417 as combination therapy. The listing for **dostarlimab** will include the crossover cohorts.

7.3. Demographic and Baseline Characteristics

The demographic characteristics sex, age, age group, ethnicity, race, race detail, height, and weight will be summarized. Age, height, and weight will be summarized using the n, mean,

standard deviation, median, minimum, and maximum. In addition, age will be categorized and summarized by ≤18, 19-64 and ≥65. The number and percentage will be computed for race, race detail, ethnicity, and sex. The demographic table will be repeated on the Enrolled analysis set, if this differs from the All Treated analysis set. Applicable age ranges to the study for the Enrolled analysis set will also be summarized using the categories: Adult (18-64 years), ≥65-84 years and ≥85 years.

The listing of demographic characteristics will include treatment group, site ID, unique subject ID, subject ID, partial date of birth, age, sex, ethnicity, race, height, and weight.

7.4. Disease Characteristics

Disease history and characteristics at initial diagnosis (including details of the tumor under study such as the primary tumor type under study, histology, histological grade, time since initial diagnosis [days], Human Papillomavirus [HPV] status, and Microsatellite Instability [MSI] status) and at study screening (including details of measurable disease at screening, stage at screening, time since last recurrence [to first exposure date], time since last progression [to first exposure date], metastatic disease at screening, time to metastatic disease [from initial diagnosis date], time since metastatic disease [to first exposure date] and metastatic disease site) will be summarized.

7.5. Concomitant Medications

Concomitant medications will be coded using the GSK Drug coding dictionary and will be listed. The listing of concomitant medications will include treatment group, site ID, unique subject ID, subject ID, ingredient, verbatim text, indication, dose, frequency, units, route, date started and study and period day, date stopped and study and period day, started prior to study (Y/N), and ongoing medication (Y/N). The listing will include information after crossover by including the crossover cohorts. Concomitant medications include any medication that was taken at some point during the on-intervention period as defined in Appendix 4, regardless of onset date.

Blood products (including platelets or red blood cells) and blood supportive care products (or growth factor support) are included in the concomitant listing.

7.6. Prior Anti-Cancer Therapy

Prior anti-cancer systemic therapies will be coded using the GSK Drug coding dictionary and will be summarized along with prior anti-cancer surgical/medical procedures. The clinical development team will adjudicate whether the systemic therapies are anti-cancer related and will classify the type of anti-cancer systemic therapy. Only systemic therapies judged as anti-cancer related are included in the displays. Only surgery/medical procedures that are classified as cancer related on the eCRF will count as anti-cancer surgical/medical procedures and will be included in the display. The table will include the following items: type of prior anti-cancer therapy (categories include, but are not limited to, chemotherapy, immunotherapy, hormonal therapy, biologic therapy, small molecule targeted therapy, vaccine, radioactive therapy and surgery), any prior checkpoint inhibitor (yes/no), intent for line of therapy, number of prior lines of anti-cancer therapy (advanced/metastatic intent only), duration of line of therapy (weeks,

advanced/metastatic intent only) and best response for last line of therapy (advanced/metastatic intent only).

Prior radiotherapy will be summarized separately. The table will include the following items: any prior radiotherapy, body site, treatment intent (options are per the eCRF), duration of radiotherapy (days) and cumulative dose (split by unit: cGy, Gy and Rad).

7.7. Palliative Radiotherapy

Palliative radiotherapy data (while on study treatment) can be viewed using RAPIDO DV - no static displays will be produced.

7.8. Follow-Up Anti-Cancer Therapies

Follow-up anti-cancer systemic therapies will be coded using the GSK Drug coding dictionary. The clinical development team will adjudicate whether the systemic therapies are anti-cancer related and will classify the type of anti-cancer systemic therapy. Only surgery/medical procedures that are classified as cancer related on the eCRF will count as anti-cancer surgical/medical procedures.

Follow-up anti-cancer therapy and follow-up radiotherapy data can be viewed using RAPIDO DV - no static displays will be produced.

8. SAFETY ANALYSES

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

Safety analyses will be based on GSK Core and Oncology Data Standards. Details of the planned displays are presented in Appendix 10: List of Data Displays. All safety summary tables will include columns for each treatment group and a total column within each Part, see Section 6.1.

8.1. Extent of Exposure

Extent of exposure will be summarized separately for GSK3745417 and dostarlimab.

Two summaries of exposure to study treatment will be produced for GSK3745417 and one summary table will be produced for dostarlimab. In the first expose table for GSK3745417 and for the exposure table for dostarlimab, the crossover cohorts will be included as separate cohorts, as per the standard approach. In the second exposure table for GSK3745417, the crossover information will be included in the display but will be included in the original monotherapy cohort (to summarise the total exposure to GSK3745417 across the monotherapy and crossover periods). In all exposure summaries, the following information will be included: dose intensity, time on study and cumulative actual dose.

The cumulative actual dose is the sum of the actual dose administered during each infusion for a participant throughout the period (GSK3745417 exposure table 1) or throughout the study (GSK3745417 exposure table 2 and dostarlimab exposure table). The cumulative actual dose will be summarized with mean, standard deviation, median, minimum, and maximum and will be categorised for GSK3745417 with the following categories: CCI [redacted]

A cycle is defined as 21 days for both Parts 1A and 2A CCI [redacted]. For GSK3745417, the number of cycles is defined as:

CCI [redacted]

- If a participant had <=4 doses of dostarlimab in total:
  (last dose date – first dose date + 21)/21
- If a participant had >4 doses of dostarlimab in total:
  (last dose date – first dose date + 42)/21

The dose intensity is calculated by 3-week periods (cycles) as the cumulative actual dose divided by the number of cycles. The dose intensity (mg/cycle) will be summarized using mean, median, standard deviation, minimum, and maximum.

The time on study treatment (weeks) will be calculated for each participant as (last dose date – first dose date + 1) /7. See Table 2 for how treatment first and last dose dates are derived for the monotherapy (Part 1A) and crossover cohorts in the three exposure tables. The time on study treatment (weeks) will be summarized with mean, standard deviation, median, minimum, and maximum and will also be categorised into the following categories: <=10 weeks, > 10 weeks to 20 weeks, > 20 weeks to 30 weeks, >30 weeks to 40 weeks and > 40 weeks.

Table 2 Treatment first and last dose dates for the monotherapy (Part 1A) and crossover cohorts in the three exposure tables

Table	Part 1A: Monotherapy	Crossover
GSK3745417 (Exposure table 1: Separate crossover cohorts)	**Start**: Monotherapy first dose date **End**: Monotherapy last dose date	**Start**: Combination (crossover) first dose date **End**: Combination (crossover) last dose date
GSK3745417 (Exposure table 2: Crossover information displayed in monotherapy cohorts)	**Start**: Monotherapy first dose date **End**: Combination (crossover) last dose date	**N/A**
Dostarlimab (Separate crossover cohorts)	**N/A**	**Start**: Combination (crossover) first dose date **End**: Combination (crossover) last dose date

Extent of exposure to GSK3745417 and dostarlimab will be listed separately, including dose intensity (mg/cycle, displayed at the participant level), start date and time of exposure, study day and period day with respect to start date, stop date and time of exposure, study day and period day with respect to stop date, scheduled dose (mg), actual dose (mg), and cumulative actual dose (mg). For GSK3745417, crossover information will be included in the listing by having two sets of rows per crossover participant: one set for GSK3745417 as monotherapy and one set for GSK3745417 as combination therapy (all will be included under the original monotherapy treatment cohort). There will also be an additional column in the listing for period (monotherapy vs. combination therapy). For dostarlimab, the crossover cohorts will be included (as per the standard approach).

8.1.1. Dose Modifications

A summary listing of overall exposure and dose modification will also be created, including component (GSK3745417 or dostarlimab), time on study treatment (weeks), dose intensity (mg/cycle), cumulative dose (mg), and a dose modification summary. Dose modification will be summarized by total number of dose delays, missed doses, dose reductions, dose escalations, infusions interrupted but completed, and infusions stopped early and not completed. Note that if a participant crosses over to combination therapy, then all dose exposure and modifications

from both the monotherapy and combination periods will be included in a single GSK3745417 component row.

8.2. Adverse Events Analyses

Adverse events analyses including the analysis of AEs, SAEs and other significant AEs will be based on GSK Core Data Standards. Summary tables will focus on treatment-emergent AEs (TEAEs) only, while listings will include all AEs (not just TEAEs). Details on treatment-emergent AEs are provided in Section 12.4.2 and the derivation for start of subsequent anti-cancer therapy is provided in Section 12.6.2. AEs will be coded using the standard MedDRA dictionary, using the latest version of the standard MedDRA dictionary at the time of the data cut-off, and grouped by system organ class (SOC). AEs will be graded by the investigator according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. All AE displays will include the crossover cohorts, unless otherwise stated. The details of the planned displays are provided in Appendix 10: List of Data Displays.

A TEAE overview summary of the number and percentage of participants with any TEAE, TEAEs related to study treatment, TEAEs leading to permanent discontinuation of study treatment, TEAE leading to dose reduction, TEAE leading to dose interruption/delay, any serious TEAEs, serious TEAEs related to study treatment, fatal serious TEAEs and fatal serious TEAEs related to study treatment will be produced.

TEAEs will be summarized by SOC, preferred term (PT), and maximum grade. The summary (and all similar summaries) will be sorted by SOC in descending order, from the SOC with the highest total incidence (summed across all treatment groups) for any AE within the class to the SOC with the lowest total incidence. The summary (and all similar summaries) 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 AE will be counted only once at the maximum grade no matter how many events they have.

A summary of non-serious TEAEs that occurred in strictly 5% of the participants or above within any treatment group will be provided (no rounding for the percentage will be used in terms of 5% threshold, e.g., event with 4.9% incidence rate should not be included in this table). The summary will be displayed in descending frequency of total incidence (of participants, summed across all treatment groups) by SOC and PT and will show both the number of participants and occurrences.

A summary table for common TEAEs (incidence greater than 10%) will be produced by decreasing total frequency. The cut off will be applied separately to Part 1A and to the combination of Part 2A and Crossover. Note if a TEAE meets the 10% threshold in **either** Part 1A **or** the combination of Part 2A and Crossover, then it will be included in the table. Note, all tables sorted by decreasing total frequency will use the total across all parts (Part 1A, Part 2A and Crossover) to determine the decreasing total frequency and will sort by alphabetic order for PTs with equal total incidence.

TEAEs related to study treatment will be summarized by SOC, PT and maximum grade. TEAEs related to study treatment will also be summarized by PT and decreasing total frequency.

A summary of non-serious TEAE related to study treatment will be summarized by PT and decreasing total frequency.

All AEs will be listed. The listing will include treatment group, site ID, unique subject ID, subject ID, age, sex, race detail, weight, DLT evaluable (Yes/No), preferred term, verbatim text, outcome, onset datetime, datetime of resolution, duration, time since first dose, time since last dose, treatment emergent (Yes/missing), maximum grade, DLT (Yes/No), serious AE (Yes/No), AE of special interest (immune-related event, cytokine release syndrome event, missing), and by related drug: relation to study treatment and action(s) taken. For the crossover cohorts, time since first dose refers to the first monotherapy dose (not the first combination [crossover] dose).

For the IB only (the team will utilise RAPIDO DV for the CSR) a listing of grade 3 and 4 AEs will be produced.

8.2.1. Adverse Events of Special Interest Analyses

For this study, the Adverse Events of Special Interest (AESI) include Cytokine Release Syndrome (CRS) events and immune-related AEs (irAEs). Infusion-related reactions (IRRs) are also of interest to the Study Team but were not included as a separate category of AESI in the protocol nor included as a separate category on the eCRF.

A summary of the number and percentage of participants with at least one treatment-emergent AESI will be provided by category, PT and maximum grade. TEAEs that satisfy at least one of the following criterium are included in the table:

1. The site indicated the AE is a CRS event on the eCRF
2. The site indicated the AE is an immune-related event on the eCRF
3. The decoded AE term is “Cytokine release syndrome”
4. The decoded AE term is “Infusion related reaction”

The table has two AESI categories, with the following selection criteria:

1. **Category**: Cytokine Release Syndrome event/Infusion Related Reaction
   Selection Criteria: Either
   a. The site indicated the AE is a CRS AESI event on the eCRF
   b. The decoded AE term is “Cytokine Release Syndrome”
   c. The decoded AE term is “Infusion Related Reaction” AND the site did not indicate that the AE is an immune-related event on the eCRF
2. **Category**: Immune-related event
   Selection Criteria: The site indicated the AE is an immune-related event on the eCRF

A summary of treatment-emergent CRS and IRR (number of participants and occurrences) will be provided. TEAEs that satisfy at least one of the following criterium are included in the table:

1. The decoded AE term is “Cytokine release syndrome”
2. The decoded AE term is “Infusion related reaction”

The following information will be included in the table:

- Number of participants with at least one CRS or IRR event
- Number of participants with at least one CRS event
- Number of CRS events reported
    - Grade 1 CRS events reported
    - Grade 2 CRS events reported
    - Grade 3-5 CRS events reported
- Number of participants with at least one IRR event
- Number of IRR events reported
    - Grade 1 IRR events reported
    - Grade 2 IRR events reported
    - Grade 3-5 IRR events reported

For the IB only (the team will utilise RAPIDO DV for the CSR) CRS events and IRRs will be listed. AEs that satisfy at least one of the following criterium are included in the listing:

1. The site indicated the AE is a CRS event on the eCRF
2. The decoded AE term is “Cytokine release syndrome”
3. The decoded AE term is “Infusion related reaction”

For the IB only (the team will utilise RAPIDO DV for the CSR) irAEs will be listed. AEs that the site indicated are immune-related on the eCRF are included in the listing.

8.2.2. Deaths and Serious Adverse Events

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’ if missing.

A summary of the number and percentage of participants and the number of occurrences of serious, study treatment related serious, fatal serious, and study treatment related fatal serious TEAEs will be created. The summary is by SOC and PT.

Serious TEAEs will be summarized by SOC, PT and maximum grade. Serious TEAEs will also be summarized by PT and decreasing total frequency.

The number and percentage of participants with serious fatal and non-fatal drug-related TEAEs will be summarized. The summary table will be displayed by PT and decreasing total frequency.

SAEs are included in the listing of all AEs. A listing of reasons for considering as a serious adverse event will be generated. The listing will include treatment group, site ID, unique subject ID, subject ID, age, sex, race detail, weight, preferred term, verbatim text, outcome, onset datetime, datetime of resolution, duration, treatment emergent (Yes/missing) and

reasons (Yes/No): resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, congenital anomaly/birth defect and other medically important serious event.

For the IB only (the team will utilise RAPIDO DV for the CSR) a listing of non-fatal serious AEs will be produced.

All deaths will be summarized based on the number and percentage of participants. This summary will classify participants by subject status (dead or alive at last contact), time of death relative to the last dose of GSK3745417 (>30 days or ≤30 days) and by the primary cause of death in the order listed in the eCRF. Note that crossover participants will be summarised in their original monotherapy cohort.

An individual participant profile of death information, as collected, will also be generated to provide specific details for participants who died, including subject details, treatment details, primary cause details, SAE record, death certificate details, course of death details, secondary cause of death details, and medical/clinical history details. The treatment at time of death, treatment sequence (monotherapy only, combination therapy only or monotherapy then combination therapy [crossover]) and period at time of death (monotherapy or combination therapy) will be included.

8.2.3. Adverse Events Leading to Discontinuation of Study Treatment and Other Significant Adverse Events

For the IB only (the team will utilise RAPIDO DV for the CSR) a listing of AEs leading to permanent discontinuation of study treatment will be produced. AEs leading to a discontinuation of either GSK3745417 or dostarlimab for the Part 2A and crossover cohorts will be included.

8.2.4. Dose Limiting Toxicity

A summary of dose-limiting toxicities during the determinative period will be provided and will be performed on the DLT evaluable population. See Section 0 for details on which participants and cohorts are included in the DLT evaluable population and what the determinative (DLT evaluable) period is for each treatment cohort. Note that the crossover cohorts do not form part of the DLT evaluable analysis set and so are excluded.

The listing of all AEs will include the Dose-Limiting Toxicity flag (Yes/No) at the AE level and the DLT evaluable flag (Yes/No) at the participant level.

8.3. Clinical Laboratory Analyses

Laboratory tests are listed the protocol Appendix 2, Table 26 and will be based on GSK Core Data Standards. The tests include hematology, chemistry, coagulation, cardiac function, thyroid function, and urinalysis tests.

All laboratory test values (excluding urinalysis) will be categorised as within the normal range, high or low with respect to normal range.

For laboratory tests which are gradable, values will be graded and reported using the CTCAE version 5.0. In some cases, there will be two bi-directional parameters (hyper- and hypo-) created and the tests will be graded by CTCAE version 5.0 in both directions.

For the following laboratory parameters, every participant will be assessed separately for low and/or high values. The following groups indicate whether laboratory severity grades are assessed according to a low value, high value, or separately for both low and high values.

• Low Value: Maximum Severity (Grade 4) for the following laboratory tests: white blood cells (WBC), neutrophils, platelets, and albumin; Normal Range only for the laboratory tests: red blood cells (RBC), haematocrit, total protein and basophils.

• High Value: Maximum Severity (Grade 4) for the following laboratory tests: alanine aminotransferase (ALT), aspartate transferase (AST), total bilirubin, alkaline phosphatase and creatinine; Normal Range only for the laboratory tests: blood urea nitrogen (BUN), and eosinophils.

• Low and High Values: Potassium, sodium, glucose, calcium, haemoglobin, lymphocytes will be assessed for the maximum severity grade for both low and high values. Monocytes will be assessed for the Normal Range only for both low and high values. For these laboratory parameters, every participant will be assessed separately for high and low values (i.e., separate summary on severity grade/normal range will be produced for high glucose (hyperglycemia) and low glucose (hypoglycemia), high potassium (hyperkalemia) and low potassium (hypokalemia), high sodium (hypernatremia) and low sodium (hyponatremia), high calcium (hypercalcemia) and low calcium (hypocalcemia), high hemoglobin (hemoglobin increased) and low hemoglobin (anemia), high lymphocytes (lymphocyte count increased) and low lymphocytes (lymphocyte count decreased) and high monocytes (monocytosis) and low monocytes (monocytopenia).

A listing of all laboratory data for participants with any value outside of normal range will be produced. The listing will include treatment group, site ID, unique subject ID, subject ID, age, sex, race detail, lab test with units, term, planned timepoint, date, study day, period day, value, normal range, change from baseline, normal range flag (Low/Normal Range/High), and grade. Crossover cohorts will be included in the listing.

A listing of urinalysis data for participants with any value of potential clinical importance will be generated. Crossover cohorts will be included in the listing.

8.3.1. Analyses of Liver Function Tests

A summary of hepatobiliary laboratory abnormalities will be provided. Crossover cohorts will be included.

When a liver stopping or monitoring event has occurred, as defined in the protocol, the Liver Event Reporting form should be completed. A liver stopping event profile will be generated and can be reviewed in RAPIDO DV along with liver restart/re-challenges data. Crossover cohorts will be available to view.

8.4. Other Safety Analyses

8.4.1. ECG

The key ECG measurement taken in this study will be the uncorrected QT interval (msec). The QT correction (QTc) will then either be calculated automatically or it will be calculated manually using the Fridericia formula (QTcF, msec). In the case QTcF is required to be calculated manually, RR interval (msec) will also be recorded on the eCRF. Additionally, an overall interpretation of the ECG reading will be provided (normal, abnormal not clinically significant, abnormal clinically significant, no result or unable to evaluate).

The QTc values based on Fridericia formula will be rounded to an integer and the values will be categorized into the following ranges: Grade 0 (<450), Grade 1 (450-480), Grade 2 (481-500), and Grade 3 (≥501). Results categorized as Grade 1 and above will be considered of potential clinical importance (PCI). The results will be categorized as 'No Change or Decrease to <450', 'Any Increase ≥450', 'Increase to ≥450 to ≤480', 'Increase to ≥481 to ≤500' and 'Increase to ≥501'.

The change from baseline in QTcF values will be categorized into the clinical concern ranges (and flagged as PCI): 31-60 and >60 msec.

ECG data can be viewed using RAPIDO DV - no static displays will be produced. Crossover cohorts will be available to view. For the numeric results recorded in triplicate, all available values will be available to view.

8.4.2. Vital Signs

Vital signs values will be categorized as follows:

- Systolic blood pressure (BP, mmHg): Grade 0 (<120), Grade 1 (120-139), Grade 2 (140-159) and Grade 3 (≥160)
- Diastolic BP (mmHg): Grade 0 (<80), Grade 1 (80-89), Grade 2 (90-99), and Grade 3 (≥100)
- Pulse rate (beats/min): Low (<60), Normal (60-100), and High (>100)
- Temperature in degrees C: 'Decrease to ≤35', Normal (36-37), 'Increase to ≥ 38'

Vital signs data can be viewed using RAPIDO DV - no static displays will be produced. Crossover cohorts will be available to view.

8.4.3. LVEF

LVEF data can be viewed using RAPIDO DV - no static displays will be produced. Crossover cohorts will be available to view.

8.4.4. Performance Status

Eastern Cooperative Oncology Group (ECOG) performance status data can be viewed using RAPIDO DV - no static displays will be produced. Data after crossover do not need to be available to view in RAPIDO DV.

8.4.5. COVID-19 Analyses

Relationship to COVID-19 will be included in the following listings:

- Listing of Reasons for Study Withdrawal
- Listing of Reasons for Study Treatment Discontinuation from GSK3745417
- Listing of Reasons for Study Treatment Discontinuation from Dostarlimab
- Listing of Important Protocol Deviations

COVID-19 infection data can be viewed using RAPIDO DV - no static displays will be produced. Data after crossover do not need to be available to view in RAPIDO DV.

8.4.6. Pregnancies

While pregnancy itself is not considered to be an AE or SAE, any pregnancy complication or elective termination of a pregnancy for medical reasons will be reported as an AE or SAE.

Pregnancy data can be viewed using RAPIDO DV - no static displays will be produced. Data after crossover do not need to be available to view in RAPIDO DV.

9. PHARMACOKINETIC ANALYSES

The PK analyses will be based on the Pharmacokinetic analysis set, unless otherwise specified. While participants will be assigned to the cohort of the actual treatment dose level received at first dosing (that is, in terms of categorisation and ordering in displays), their PK data will be summarized by the actual dose received for each visit.

Note that PK analyses will only be performed on GSK3745417 and not on dostarlimab. PK summary tables will include columns for treatment groups only (a total column within each Part will not be included). Refer to Section 12.5.3 for PK reporting standards. Crossover cohorts will be included in all PK displays where space allows (some figures are restricted to certain visits, so may not include crossover visits).

9.1. Drug Concentration Measures

Blood sampling time will be related to the start of dosing.

GSK3745417 plasma serum concentration-time data will be listed by treatment group. The listing will include treatment group, site ID, unique subject ID, subject ID, age, sex, race detail, visit, date, study day, period day, actual dose (mg), planned relative time, actual time, time deviation, actual relative time, lower limit of quantification (LLQ) value for the assay, concentration results and PK analysis exclusion flag. Values below the LLQ are recorded as Not Quantifiable (NQ), see Section 12.5.3.

The PK analysis exclusion flag indicates which samples are excluded from the PK concentration tables and figures and the PK parameter analysis. In general, the following samples will be excluded:

- Where VISITNUM is missing.
- When PCDTC is missing.
- Pre-treatment pre-dose records (e.g. Week 1) with quantifiable results: pre-treatment pre-dose records should have NQ and those records are included in the PK concentration tables and figures.
- Post-treatment pre-dose records (e.g. Week 2+) with higher PK concentration than final record from previous treatment cycle (e.g. Week 1 EOI+24 HR)

The final list of exclusions (that is, samples that will have the PK analysis exclusion flag as "Yes") will be provided by CPMS.

GSK3745417 plasma concentration-time data will be summarized by treatment and nominal time using descriptive statistics (n, number imputed, mean, 95% confidence interval [CI], standard deviation [StD], median, minimum, and maximum). If more than 30% of values at a time-point are imputed, then standard deviation will not be reported.

Linear and semi-logarithmic individual concentration-time profiles (by treatment and participant) and mean (+StD) and median profiles by GSK3745417 dose will be plotted.

For the table and figures, NQ values will be imputed as per Section 12.5.3.

Urine concentration data will be made available in RAPIDO DV, see Section 1, when available for participants.

9.1.1. Lower Limit of Quantification (LLQ) values

Three assays were used for PK analysis in this study, with each assay having its own LLQ. In general, the following assays and LLQs were used:

- Samples analyzed prior to June 2019: assay with LLQ of 0.005 ng/mL.
- Samples analyzed from June 2019 to August 2020: assay with LLQ of 5 ng/mL.
- Samples analyzed after August 2020: assay with LLQ of 0.1 ng/mL.

In general, the time of the analysis determined the assay, and therefore, the same assay may not have been used for all samples from a participant. There may have been exceptions to the general guidance above, and the concentration-time listing will include the LLQ value for the assay used for each measurement.

9.2. Derived Pharmacokinetic Parameters

9.2.1. Variables

Pharmacokinetic parameters for GSK3745417 administered intravenously in this study will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of Phoenix WinNonlin.

All calculations of non-compartmental PK parameters will be based on actual sampling times. For each participant and for each dose, additional pharmacokinetic parameters may be derived as described in Table 3 will be determined from the GSK3745417 plasma serum concentration-time data, as data permit.

Table 3 Derived Pharmacokinetic Parameters

Parameter	Parameter Description
AUC(0-t)	Area under the plasma/serum concentration-time curve from time zero to the time of the last quantifiable concentration (C(t)) will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC(0-tau)	Area under the plasma/serum concentration-time curve during the dosing interval using the linear/log trapezoidal rule.
AUC(0-inf)	For single dose. Area under the plasma/serum concentration-time curve from time zero extrapolated to infinity will be calculated as: AUC(0-inf) = AUC(0-t) + C(t) / lambda_z
%AUCex	For single dose. The percentage of AUC (0-inf) obtained by extrapolation (%AUCex) will be calculated as: [AUC(0-inf) – AUC(0-t)] / AUC(0-inf) x 100

Parameter	Parameter Description
Cmax	Maximum observed plasma/serum concentration, determined directly from the plasma/serum concentration-time data.
Lambda_z	Terminal phase elimination rate constant. For single dose. The lambda_z lower and upper limits and number of points used to determine lambda_z will also be reported.
tmax	Time to reach Cmax, determined directly from the plasma/serum concentration-time data.
t½	For single dose. Apparent terminal phase half-life will be calculated as: t½ = ln2 / lambda_z
tlast	Last time point where the concentration is above the limit of quantification
CL	Clearance CL=dose / AUC(0-inf)
CLss	Steady-state Clearance CLss=dose/AUC(0-tau) for multiple dose
Vz	Volume of distribution Vz=dose/ (λz x AUC(0-inf)) for single dose; Vz=dose/(λz x AUCtau) for multiple dose
Vdss	Volume of distribution at steady-state Vdss = CL x MRT_{IV} for single dose Or Vdss = CLss x MRT_{IV} for multiple dose
$AR_{0,AUC}$	$AR_{0,AUC} = AUC(0\text{-}tau)_{week4}/AUC(0\text{-}tau)_{week1}$
$AR_{0,Cmax}$	$AR_{0,Cmax} = Cmax_{week4}/Cmax_{week1}$

NOTES:
- Additional parameters may be included, as required.

AUC(0-inf) will be reported if <20% of this area comes from extrapolation. However, if >40% of the AUC has been extrapolated, AUC(0-inf) data may not be reported.

9.2.2. Summary Measures

All derived PK parameters will be listed. The listing will include treatment group, site ID, unique subject ID, subject ID, age, sex, race detail, analysis visit, actual dose (mg) and the PK parameters listed in **Table** 3.

All derived PK parameters will be summarised descriptively by treatment. For each of these parameters, except Tmax, the following summary statistics will be calculated for each dose

level: median, minimum, maximum, arithmetic mean, 95% CI for the arithmetic mean, StD, between subject coefficient of variation (%CVb = 100*(sqrt (exp(SD^2) - 1))) (where SD = SD of natural log transformed data), geometric mean (the n^{th} root of the product of the n values), 95% CI for the geometric mean and standard deviation of the log- transformed data. For Tmax, median, maximum, minimum, arithmetic mean, 95% CI, and standard deviation will be calculated.

All PK parameters will be reported to at least 3 significant digits, but to no more significant digits than the precision of the original data.

The following pharmacokinetic statistical analyses will only be performed if sufficient data are available (i.e., if participants have well defined serum profiles). A minimum of 3 doses will be required to assess dose proportionality (across all treatment cohorts). Analyses may not be performed on Cmax or AUC if the team considers there are a large amount of data either below the limit of quantification or non-calculable for at least one of the three doses.

Dose proportionality of GSK3745417 will be assessed by visual inspection of:

- Scatter plots (+geometric mean and 95% CI, as appropriate) of GSK3745417 dose-normalized PK parameter vs dose for AUC(0-∞) [or if not calculable for the majority of participants, then AUC(0-t)] and Cmax

The PK parameters will be dose-normalized by the actual dose that each participant received (i.e. Cmax/actual dose).

Analysis procedures will follow *Non-Compartmental Analysis of Clinical Pharmacokinetic Data* (VQD-REF-015788 [1.0]) and GSK PK Display Standards unless otherwise noted.

10. EFFICACY ANALYSES

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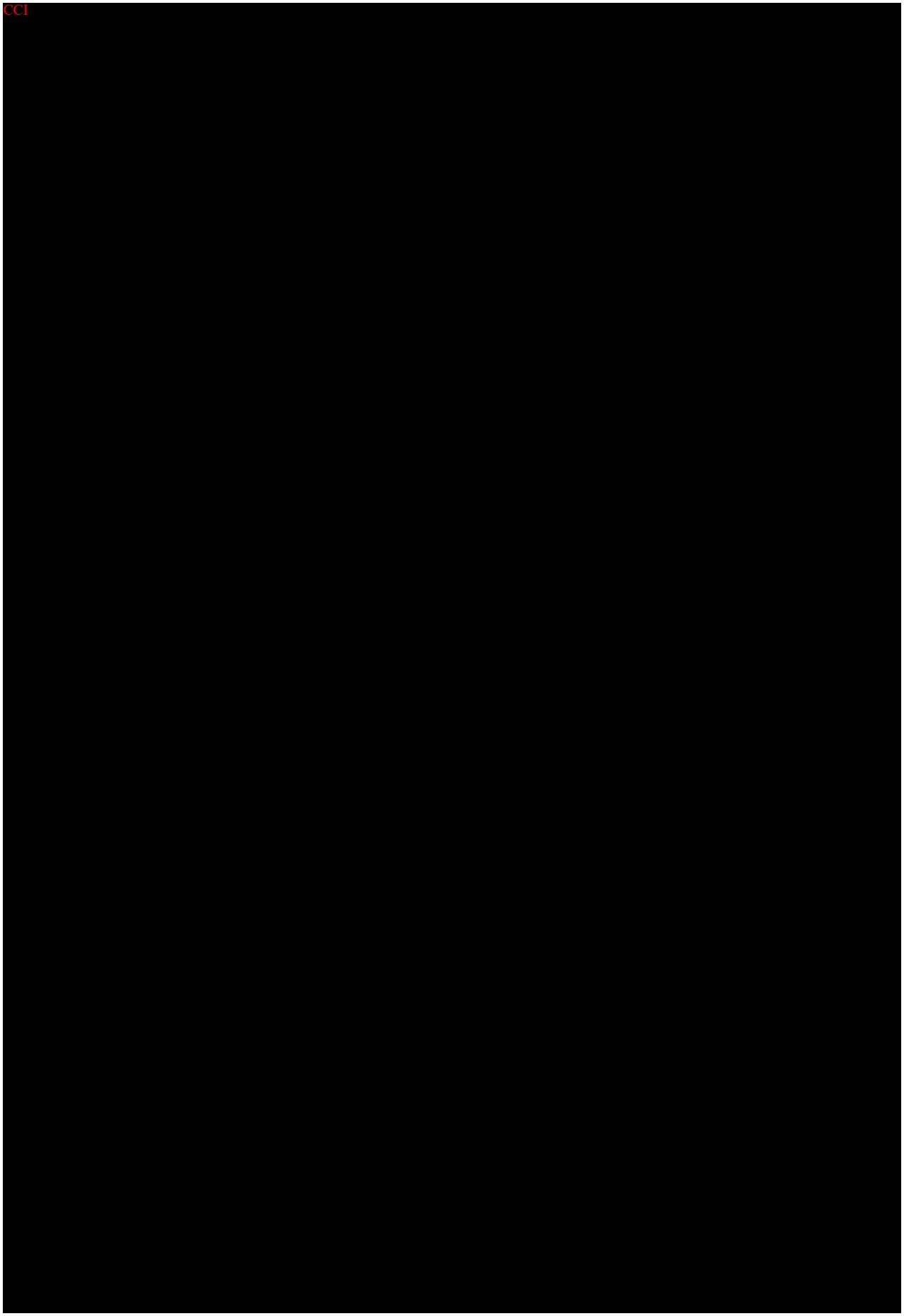

CCI

CCI

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Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, et al. New response evaluation criteria in solid tumors: Revised RECIST guidelines (version 1.1). Eur J Cancer. 2009;45(2):228-247.

12. APPENDICES

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

12.1.1. Exclusions from Per Protocol Population

There is no planned per protocol analysis for this study.

12.2. Appendix 2: Schedule of Activities

12.2.1. Protocol Defined Schedule of Events

See protocol Section 1.2 Schedule of Activities for detailed schedule of activities for each part.

12.3. Appendix 3: Assessment Windows

12.3.1. Definitions of Assessment Windows for Analyses

For PK data, the unscheduled timepoints will be slotted as below. For the remaining endpoints, data will be summarized by the nominal visits.

Elapsed time from dose to start of PK sample collection (ARELTM) in hours is calculated as = (start datetime of PK sample collection – reference dose datetime) /3600.

Elapsed time from dose to start of PK sample collection (ARELTM) in minutes is calculated as = (start datetime of PK sample collection – reference dose datetime) /60.

Slotting algorithm if elapsed time (ARELTM) is in minutes

- 0 < ARELTM <= 5, ARELTM = 5 min
- 13 <= ARELTM <= 17, ARELTM = 15 min
- 25 <= ARELTM <= 35, ARELTM = 30 mins
- 40 <= ARELTM<= 50, ARELTM = 45 mins

Slotting algorithm if elapsed time (ARELTM) is in hours

- 0.75 <= ARELTM <= 1.25, ARELTM = 1 hr
- 1.50 <= ARELTM <= 2.50, ARELTM = 2 hrs
- 3.5 <= ARELTM <= 4.5, ARELTM = 4 hrs
- 5 <= ARELTM <= 7, ARELTM = 6 hrs
- 7 <= ARELTM <= 9, ARELTM = 8 hrs
- 11 <= ARELTM <= 13, ARELTM = 12 hrs
- 16 <= ARELTM <= 20, ARELTM = 18 hrs
- 22 <= ARELTM < =26, ARELTM = 24 hrs

12.4. Appendix 4: Study Phase and Treatment Emergent Flag for Adverse Events

12.4.1. Study Phase

Assessments and events will be classified according to the time of occurrence relative to study intervention period.

Pre-Intervention is defined as time prior to the first dose of study intervention.

On-Intervention is defined as time from first dose to last dose plus 30 days. If time of assessment or study intervention is not collected, the following assessment on the first dose date will be assumed to be taken prior to the first dose and therefore considered pre-intervention: ECOG, ECG, lab, and vital signs, and first dose date is considered on-intervention for AE and concomitant medication.

Post-Intervention is defined as any time post on-intervention window, i.e. date > last dose date + 30 days.

12.4.1.1. Study Phases for Anti-Cancer Therapy

This table should be used for anti-cancer systemic therapy, anti-cancer surgical/medical procedures and radiotherapy.

Study Phase	Definition
Prior	If anti-cancer therapy start date is not missing and is before the first dose of study intervention OR If anti-cancer therapy start date is missing and: • The anti-cancer systemic therapy comes from the Prior Anti-Cancer Therapy eCRF page. • The anti-cancer surgical/medical procedure comes from the Prior Medical/Surgical procedures eCRF page. • The radiotherapy comes from the Anti-Cancer Radiotherapy eCRF page.
On Treatment	If anti-cancer therapy start date is not missing and is on or after the first dose and before the last dose of study intervention (if anti-cancer therapy start day is on the same day as first dose then anti-cancer therapy is assumed to have been taken/performed after first dose) OR If anti-cancer therapy start date is missing and: • The radiotherapy comes from the Anti-Cancer Radiotherapy On Treatment eCRF page.
Follow-up	If anti-cancer therapy start date is not missing and is on or after the last dose of study intervention (if anti-cancer therapy start day is on the same day as last dose then anti-cancer therapy is assumed to have been taken/performed after last dose) OR If anti-cancer therapy start date is missing and:

Study Phase	Definition
	• The anti-cancer systemic therapy comes from the Follow Up - Anti-Cancer Therapy eCRF page. • The radiotherapy comes from the Follow Up – Radiotherapy eCRF page.

12.4.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	For AEs (which are not SAEs and not AESIs) in GSK3745417 monotherapy cohorts: • Monotherapy participants who do not crossover: Study Treatment Start Date ≤ AE Start Date or pre-existing (prior to exposure) AE Worsening Date ≤ Treatment Discontinuation Visit (TDV) or Study Treatment Stop Date + 30 Days if TDV is missing. • Monotherapy participants who crossover: Monotherapy Study Treatment Start Date ≤ AE Start Date or pre-existing (prior to exposure) AE Worsening Date ≤ Monotherapy TDV or the earliest of (Monotherapy Study Treatment Stop Date + 30 Days, Crossover Date) if TDV is missing. • AE Start Date is missing. For AEs (which are not SAEs and not AESIs) in GSK3745417 + dostarlimab combination cohorts: • Study Treatment Start Date ≤ AE Start Date or pre-existing (prior to exposure) AE Worsening Date ≤ TDV or Study Treatment Stop Date + 30 Days if TDV is missing. • AE Start Date is missing Note that AE worsening date is included in the definition of AE start date in the eCRF and so no programming is required. For AEs (which are not SAEs and not AESIs) in GSK3745417 + dostarlimab **crossover** cohorts: • (Crossover) Combination Study Treatment Start Date ≤ AE Start Date or AE Worsening Date for AE that started during the GSK3745417 monotherapy cohort ≤ (Crossover) Combination TDV or (Crossover) Combination Study Treatment Stop Date + 30 Days if TDV is missing. • AE Start Date is missing Note, if a participant has an AE while on monotherapy and crosses over to combination therapy prior to the AE resolving:

Flag	Definition
	• If the AE does not worsen, the AE will only be counted in the monotherapy cohort. • If the AE does worsen, then the AE will be counted in both the monotherapy cohort and the crossover combination cohort. Note that TDV date is taken as the latest TDV assessment date. For SAEs/AESIs in GSK3745417 monotherapy cohorts: • Monotherapy participants who do not crossover: Study Treatment Start Date ≤ SAE/AESI Start Date or pre-existing (prior to exposure) SAE/AESI Worsening Date ≤ Study Treatment Stop Date + 90 days or Start of Subsequent Anti-Cancer Therapy, whichever occurs first • Monotherapy participants who crossover: Study Treatment Start Date ≤ SAE/AESI Start Date or pre-existing (prior to exposure) SAE/AESI Worsening Date ≤ the earliest of (Study Treatment Stop Date + 90 days, Start of Subsequent Anti-Cancer Therapy, Crossover Date) • SAE/AESI Start Date is missing For SAEs/AESIs in GSK3745417 + dostarlimab combination cohorts: • Study Treatment Start Date ≤ SAE/AESI Start Date or pre-existing (prior to exposure) SAE/AESI Worsening Date ≤ Study Treatment Stop Date + 90 days or Start of Subsequent Anti-Cancer Therapy, whichever occurs first • SAE/AESI Start Date is missing For SAEs/AESIs in GSK3745417 + dostarlimab **crossover** cohorts: • (Crossover) Combination Study Treatment Start Date ≤ SAE/AESI Start Date or SAE/AESI Worsening Date for SAE/AESI that started during the GSK3745417 monotherapy cohort ≤ (Crossover) Combination Study Treatment Stop Date + 90 days or Start of Subsequent Anti-Cancer Therapy, whichever occurs first. • SAE/AESI Start Date is missing CCI [redacted]

NOTES:

- Treatment emergent SAEs/AESIs, as per this definition, are included in the summary tables of TEAEs.
- See Section 12.6.2 for definition of start of subsequent anti-cancer therapy.

- Note, if a participant crosses over to combination therapy before an AE is resolved, the actual AE end date should still be populated in the AE listings for the monotherapy cohort (regardless of whether the AE worsened on crossover combination therapy).
- As per the protocol, SAEs that are related to study participation will be collected from the time of consent. Note that these will be included in listings (as listings include all AEs), however, will not be included in the tables (as tables only include treatment related AEs).

12.5. Appendix 5: Data Display Standards & Handling Conventions

12.5.1. Reporting Process

Software	
• Prior to October 2023: The latest supported versions of SAS and R software were used. • October 2023 onwards: Latest versions of METEOR and Domino with in-built containers for SAS and R environments will be used. • As of the 22-Mar-2024, the current versions are METEOR v4.0 and Domino v5.7.1.	
Reporting Area (prior to October 2023)	
HARP Server	: US1SALX00259
HARP Compound	: Compound: GSK3745417, Study: mid208850
Reporting Area (October 2023 onwards)	
GitHub Repository	gsk_tech/52018_208850 (github.com)
METEOR	IB: 52018_208850_ISRC_<<X>> CSR: 52018_208850_EOS
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (ADaM Version 2.1 and ADaM IG Version 1.1).	
Generation of RTF Files	
• RTF files will be generated for all summary tables	

12.5.2. Reporting Standards

General

• The current GSK Statistical Display Standards will be applied for reporting, unless otherwise stated (Library Location: https://myteams.gsk.com/:w:/r/sites/IDSLLibrary):
  • Section 4: Principles for All Displays
  • Section 5: Principles for Data Listings
  • Section 6: Principles for Summary Table
  • Section 7: Principles for Graphics
GSK Statistical Display Principles will be followed in the creation of GSK standard and non-standard outputs

Formats
• GSK IDSL Statistical Principles 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. • Summary Statistics: values will be reported relative to the precision on the eCRF. Min and max will be to the same as the raw data, mean and median to 1 extra decimal place, standard deviation to 2 extra decimal places. • Listings: values will be displayed to the same precision on the eCRF

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 listings: o Planned and actual time relative to study drug dosing will be shown in listings. o Unscheduled or unplanned readings will be presented within the participant listings.	
Unscheduled Visits	
• Unscheduled visits will not be included in summary tables and/or figures except for worst-case post – baseline analysis and PK data. For PK Unscheduled visits, compare the PK collection time with the corresponding treatment prior to collection of PK. If the PK start date is greater than the latest previous exposure date and less than the immediate next exposure date, then unscheduled PK record will be slotted into the week of previous exposure date. For e.g. if there is an unscheduled PK collection after WEEK 2 treatment exposure and before WEEK 3 treatment exposure, then the unscheduled PK record will be slotted into WEEK 2. • Unscheduled timepoints that fall outside of the protocol defined timepoints after slotting will not be included in the reporting of summary tables for PK. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to GSK Statistical Display Standards Section 6.6
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to GSK Statistical Display Standards Section 7	

12.5.3. Reporting Standards for Pharmacokinetic

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 (CPMS) function will be created according to the "Standards for the Reporting of PK data using HARP" and "Extraction and Analysis of Pharmacokinetics Data" documents. Note: Concentration values will be imputed as per *Non-Compartmental Analysis of Clinical Pharmacokinetic Data* (VQD-REF-015788 [1.0]), Section 2.2.3.
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Note: Concentration values will be imputed as per *Non-Compartmental Analysis of Clinical Pharmacokinetic Data* (VQD-REF-015788 [1.0]), Section 2.2.3 for descriptive summary statistics/analysis and summarized graphical displays only. In the

	listing, NQ values will be reported as NQ and the LLQ for the assay will be given (no imputation will be performed).
Pharmacokinetic Parameter Data	
Is NQ impacted PK Parameters Rule Being Followed	*Yes, refer to Non-Compartmental Analysis of Clinical Pharmacokinetic Data* (VQD-REF-015788 [1.0]), Section 2.3.6.
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Refer to *Non-Compartmental Analysis of Clinical Pharmacokinetic Data* (VQD-REF-015788 [1.0]), Section 2.3.6.

12.6. Appendix 6: Derived and Transformed Data

12.6.1. 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 except for PK. For PK data, if there are multiple records observed at the same date and time for a participant, those data will be excluded from the WNL file and will not be used for the derivation of PK parameters.

- If there are two values within a time window (as per Section 12.3.1) 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.

- PK concentration samples that are duplicated based on the same USUBJID, VISIT, PCTPT and PCDTC variables, are excluded from all PK analyses and displays, including the PK concentration listing, as the duplication is an error. That is, only one unique record according to USUBJID, VISIT, PCTPT, PCDTC and PCORRES is included.

Study Day and Period Day

Study Day:

- Study Day is calculated as the number of days from First Dose Date:
  - Ref Date = Missing → Study Day = Missing
  - Ref Date < First Dose Date → Study Day = Ref Date – First Dose Date
  - Ref Date ≥ First Dose Date → Study Day = Ref Date – (First Dose Date) + 1

Period Day:

- For monotherapy participants who do not crossover, or for participants who join the study in Part 2A/the Imaging Sub-study: the Period Day is the same as the Study Day.
- For participants who cross over from monotherapy to combination therapy:
  - Monotherapy period: Period Day is the same as the Study Day.
  - Combination (crossover) period: Period Day is calculated as the number of days from First **Combination** Dose Date, using the same logic as above.

Change from Baseline

- Change from Baseline = Post-Baseline Visit Value – Baseline
- % Change from Baseline= 100 x (Post-Baseline Visit Value – Baseline) / Baseline
- Maximum Increase/Decrease from Baseline = maximum (Increase/Decrease from Baseline)
- If either the Baseline or Post-Baseline Visit Value is missing, Change from Baseline and % Change from Baseline is set to missing

12.6.2. Study Population

Treatment Assignment

- As defined in Section 0, in the All Treated analysis set participants will be assigned to the cohort of the first dose they received, regardless of any permanent dose reductions or regimen changes. This will be derived from exposure data.
- If the dose level is reduced or the dose regimen changes during the treatment period from what the participant initially received, study population and safety data will be summarized by the dose level the participant initially received. However, PK data will be summarized by the actual dose received for each visit, see below.
- The most common dose regimen change (within either Part 1A or Part 2A) is expected to be a reduction in frequency, that is, reduction from Q1W dosing to Q3W dosing.
- Data on participants who have crossed over from Part 1A to Part 2A will generally be presented separately in crossover cohorts, see Section 6.1.3 for details.

- **Treatment Assignment: PK**

- For PK summaries and analyses, participants are assigned to the cohort of the actual dose received at that visit.
- CCI [redacted]
- Participants who receive <90% of the planned dose level for a specified visit will have their data excluded from the relevant tables and figures for that visit (as it cannot be assigned to an existing cohort).
- CCI [redacted]
  schedule while they are on monotherapy. This is due to a limitation in data collection, as regimen change during the study was not collected on the eCRFs. Due to the short half-life of GSK3745417, this treatment assignment approach should have a negligible impact on the PK analyses.

Time since Initial Diagnosis

- Calculated as the number of [Days] from the Date of Initial Diagnosis:
  - First Dose Date = Missing → Elapse Time = Missing
  - Date of Initial Diagnosis = Completely/partially Missing → Elapse Time = Missing
  - Otherwise → Elapse Time = First Dose Date – Date of Initial Diagnosis + 1

Start of Subsequent Anti-Cancer Therapy

- The start of subsequent anti-cancer therapy is defined as the first anti-cancer therapy taken on the same day as or after the last dose of treatment.
- The following records are included for consideration of anti-cancer therapy:
  - **Systemic therapy**: Any systemic therapy, as adjudicated by the clinical team.

- **Medical/surgical procedures**: Any medical/surgical procedure, which is classified as "Cancer related" on the eCRF.

12.6.3. Safety

Adverse Events

Duration of AE

- Calculated as the number of [days] from AE Start Date to AE Stop Date:
  - AE Start Date = Missing → Elapse Time = Missing
  - AE Stop Date = Missing → Elapse Time = Missing
  - Otherwise → Elapsed Time = AE Stop Date – AE Start Date + 1

Extent of Exposure

- Number of weeks of exposure to study drug will be calculated based on the formula:

Duration of Exposure in Weeks = [last dose date – first dose date + 1] /7

- The cumulative dose will be based on the formula:

Cumulative Dose = Sum of (the actual dose administered during each infusion)

- The infusion dose intensity is the cumulative dose divided by the number of 3-week periods (cycles) across the entire treatment period.

- For GSK3745417:

Q1W: Dose intensity = Cumulative Dose/((last dose date – first dose date + 7)/21)
Q3W: Dose intensity = Cumulative Dose/((last dose date – first dose date + 21)/21)

- For dostarlimab:
  - If a participant had **<=4 doses** of dostarlimab in total:
    Dose intensity = Cumulative Dose/ (last dose date – first dose date + 21)/21
  - If a participant had **>4 doses** of dostarlimab in total:
    Dose intensity = Cumulative Dose/ (last dose date – first dose date + 42)/21

Corrected QT Intervals

When not entered directly in the eCRF, corrected QT intervals using Fredericia's (QTcF) formula will be calculated, in msec, using QT and the RR interval:

$$QTcF = QT/\sqrt[3]{(RR/1000)}$$

12.6.4. Crossover

The date (and time, where applicable) of crossover is defined as the date (and time) of the first dose of combination therapy for participants who were initially assigned monotherapy.

12.7. Appendix 7: Reporting Standards for Missing Data

12.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Participants will be considered to have completed the DLT portion of the study if they complete screening assessments and receive at least 1 study treatment and experience a DLT during the 21 or 29-day DLT observation period or complete the DLT observation period. • A participant will be considered to have completed the study if the site indicated on the eCRF that they did not discontinue the study before completing the follow up. o Under Protocol Amendment 7, the required follow-up period is until 90 days after last dose, starting subsequent anti-cancer therapy or dying. Participants who are in follow-up at the time of Protocol Amendment 7 and have been followed for at least 90 days are considered as having completed the follow-up period. o Prior to Protocol Amendment 7, the required follow-up period was 2 years from first dose (or until death). • 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. • If a participant withdraws from the study before completion of the DLT period for reasons other than DLT, the participant will not be counted as DLT evaluable and 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. • If PACT is initiated, participants who transition to PACT will be considered as ongoing in the study.

12.7.2. 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 using 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.

Element	Reporting Detail
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.

12.7.2.1.Handling of Missing and Partial Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in participant listing displays.
Adverse Events	CCI [redacted]

Element	Reporting Detail
	CCI [redacted]
Concomitant Medications/ Medical History	
Prior Anti-cancer Systemic	

Element	Reporting Detail
Therapy/ Radiotherapy/ Surgical Procedures	CCI [redacted]
Follow-up Anti-cancer Systemic Therapy (as adjudicated by the clinical team)/Cancer related Surgical Procedures for Efficacy Evaluation (BOR) and TEAE definition	
Other Follow-up Anti-cancer Systemic Therapy/ Radiotherapy/ Non-cancer related Surgical Procedures	
On-treatment Radiotherapy	CCI [redacted]

12.7.2.2. Handling of Missing Dates in terms of crossover

This sub-section describes which period (that is, monotherapy or crossover combination therapy) events should be included in for crossover participants when either the start or end date of the event is missing.

Concomitant medication

Note that the only concomitant display to be produced is a listing.

Concomitant Medication Start Date	Concomitant Medication End Date	Cohort Inclusion Rule
Before crossover	Before crossover	Include in monotherapy cohort only
Before crossover	After crossover	Include in both monotherapy and crossover cohort
Before crossover	Missing	Include in both monotherapy and crossover cohort
After crossover	After crossover	Include in crossover cohort only
After crossover	Missing	Include in crossover cohort only
Missing	Before crossover	Include in monotherapy cohort only
Missing	After crossover	Include in both monotherapy and crossover cohort
Missing	Missing	Include in both monotherapy and crossover cohort

12.8. Appendix 8: Values of Potential Clinical Importance

To identify values of potential clinical importance, CTCAE version 5.0 will be used to assign grades for laboratory parameters including clinical chemistry, hematology, liver function tests and vital signs (blood pressure, temperature). For urinalysis, a participant is considered to have urinalysis results of PCI, if there is an increase in Protein or an increase in Occult Blood results during the study, or if microscopy is performed.

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.

12.8.1. ECG

ECG Parameter	Units		Clinical Concern Range	
			Lower	Upper
	Absolute			
Absolute QTcF Interval	msec	Grade 1	≥ 450	< 481
		Grade 2	≥ 481	< 501
		Grade 3	≥ 501	
	Change from Baseline			
Increase from Baseline QTcF	msec		> 30	≤ 60
	msec	Grade 3	> 60	

12.8.2. Vital Signs

Vital Sign Parameter (Absolute)	Units		Clinical Concern Range	
			Lower	Upper
Systolic Blood Pressure	mmHg	Grade 1	≥120	<140
	mmHg	Grade 2	≥140	<160
	mmHg	Grade 3	≥160	
Diastolic Blood Pressure	mmHg	Grade 1	≥ 80	< 90
	mmHg	Grade 2	≥ 90	< 100
	mmHg	Grade 3	≥ 100	
Heart Rate	bpm	L/H	< 60	> 100
Temperature	Degrees C	L/H	≤ 35	≥ 38

12.9. Appendix 9: Abbreviations & Trademarks

12.9.1. Abbreviations

Abbreviation	Description
AE	Adverse Event
AESI	Adverse Event of Special Interest
ALT	Alanine Aminotransferase
AST	Aspartate Transferase
AUMC	Amsterdam University Medical Centers
BLRM	Bayesian Logistic Regression Model
BOR	Best Overall Response
BP	Blood Pressure
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
CR	Complete Response
CRS	Cytokine Release Syndrome
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
DBF	Database Freeze
DBR	Database Release
DEM	Dose Escalation Meeting
DLT	Dose Limiting Toxicity
DM	Data Management
DP	Decimal Place
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
GSK	GlaxoSmithKline
HPV	Human Papillomavirus
IB	Investigator Brochure
IDSL	Integrated Data Standards Library
irAE	Immune-Related Adverse Event
IRR	Infusion-Related Reaction
LLQ	Lower Limit of Quantification
LVEF	Left Ventricular Ejection Fraction
MSI	Microsatellite Instability
MTD	Maximum Tolerated Dose
NA	Not Applicable
NE	Not Evaluable
NQ	Non-Quantifiable
CCI [redacted]	
PACT	Post Analysis Continuation of Treatment
PCI	Potential Clinical Importance

Abbreviation	Description
PD	Progressive Disease
PK	Pharmacokinetic
PK/PD	Pharmacokinetics/Pharmacodynamics
PR	Partial Response
PT	Preferred Term
Q1W	Every 1 week
Q3W	Every 3 weeks
Q6W	Every 6 weeks
QTc	QT Correction
QTcF	Fridericia's QT Correction
RAP	Reporting & Analysis Plan
RBC	Red Blood Cells
RECIST	Response Evaluation Criteria in Solid Tumours
RP2D	Recommended Phase 2 Dose
S&P	Statisticians and Programming
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SD	Stable Disease
SDTM	Study Data Tabulation Model
SERM	Safety Evaluation and Risk Management
SOC	System Organ Class
StD	Standard Deviation
TDV	Treatment Discontinuation Visit
TEAE	Treatment-Emergent Adverse Event
TLF	Table, Listing, Figure
TMF	Trial Master File
WBC	White Blood Cells

12.9.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
HARP

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS
WinNonLin

12.10. Appendix 10: List of Data Displays

12.10.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.n	1.1 to 1.n
Safety	3.1 to 3.n	3.1 to 3.n
Pharmacokinetic	4.1 to 4.n	4.1 to 4.n
Efficacy	6.1 to 6.n	6.1 to 6.n
Section	**Listings**	
ICH Listings	1 to 23	
Other Listings	24 to 25	

12.10.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Section 12.10: 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
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln

12.10.3. Deliverables

Delivery	Description
IB	Investigator Brochure Update
DEM	Dose Escalation Meeting (Part 1A)
SAC	(CSR) Statistical Analysis Complete

Note for Programmers:

Analyses will be reported by actual treatment dose level received at first dosing, except PK analyzes where data will be summarized by the actual dose received for each visit.

Include dose levels from both Part 1A and Part 2A in all the displays unless otherwise stated. Include total for all the tables (except PK tables) and the total should be separate for Part 1A, Part 2A and Crossover (when included). It should not be combined unless otherwise stated. For all the summary tables, cluster all the dose levels within Part 1A and dose levels within Part 2A as provided in the mock shell. All listings will be sorted by Treatment, site ID, unique subject ID, subject ID and then by date and time, if applicable. Include treatment as a header in each

page of the listing as provided in the mock shell. Include site ID, unique subject ID and subject ID in a stacked column for all the listings as provided in the mock shell.

Some listings were only produced statically for the IB and the data will be available to view in RAPIDO DV for the CSR SAC.

12.10.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.1.	All Treated	ES8	Summary of Subject Status and Subject Disposition for the Study Conclusion Record	Use sentence case for text in the template. Do not use upper case. Split Part 1A into Part 1A Non-Crossover and Part 1A Crossover. Use the crossover cohorts in Part 1A Crossover. Use reasons for study withdrawal from eCRF, not from the standard. Participants are included in the "Ongoing: On study treatment" row if the reason for study discontinuation was "Protocol-defined stopping criteria" and the specify variable (upper case) contained both the strings "PACT" and "CONTINUING TREATMENT". Participants are included in the "Ongoing: In follow-up" row if the reason for study discontinuation was "Protocol-defined stopping criteria" and the specify variable (upper case) contained both the strings "PACT" and "90 DAY SAFETY FOLLOW-UP".	SAC

				The following footnotes only should be included: "Note: Participants who were initially recruited to Part 1A and subsequently initiated GSK3745417 + Dostar are included only in the relevant Part 1A Crossover cohort, where the table reflects their status and primary withdrawal reason related to their GSK3745417 + Dostar therapy." Completed follow-up [1]: "[1] Site indicated that the participant did not discontinue the study before completing all follow-up." Ongoing [2]: "[2] Participants are continuing the study as part of the Post Analysis Continuation of Treatment (PACT)". Primary reason [3]: "[3] Subjects may have only one primary reason." Protocol-defined stopping criteria [4]: "[4] Sites were asked to complete the end of study CRF form with this reason for study discontinuation for participants who entered PACT. As such, this category includes X participants who entered PACT (have subject status as 'Ongoing')." X should be derived.	
1.2.	Enrolled	ES8	Summary of Subject Status and Subject Disposition for the Study Conclusion Record	Note: This is a placeholder. Only to be created when Enrolled Population is different from All Treated Population.	SAC

				If this table is required, repeat all notes as above table.	
1.3.	All Treated	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment for GSK3745417	Use sentence case for text in the template. Do not use upper case. Include Crossover sub-category for Discontinued for Part 1A Treatments only. Add footnote [1] after "Ongoing": "[1] Participants are continuing study treatment as part of the Post Analysis Continuation of Treatment (PACT) phase". Remove original footnotes [2] and [3]. Add footnote: "'Note: if a participant initiated GSK3745417 + Dostar combination therapy following GSK3745417 monotherapy (crossed over) then details regarding the GSK3745417 monotherapy are included in the relevant Part 1A monotherapy cohort and details regarding the GSK3745417 + Dostar combination therapy are included in the relevant crossover cohort"	SAC
1.4.	All Treated	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment for Dostarlimab	Use sentence case for text in the template. Do not use upper case. Include dose levels from Part 2A and crossover only. Add footnote [1] after "Ongoing": "[1] Participants are continuing study treatment as	SAC

				part of the Post Analysis Continuation of Treatment (PACT) phase". Remove original footnotes [2] and [3].	
1.5.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure	Reasons for failure to match values and order from eCRF.	SAC
1.6.	Enrolled	NS1	Summary of Number of Subjects by Country and Site ID	Add a total column (total over all participants from both Part 1A and 2A).	SAC
1.7.	All Treated	NS1	Summary of Number of Subjects by Country and Site ID	Add a total column (total over all participants from both Part 1A and 2A). Note: This is a placeholder. Only to be created when Enrolled Population is different from All Treated Population.	SAC
Protocol Deviation					
1.8.	All Treated	DV1	Summary of Important Protocol Deviations	Include crossover cohorts.	SAC
Demographic Characteristics					
1.9.	All Treated	DM1	Summary of Demographic Characteristics	Add a total column (total over all participants from both Part 1A and 2A). Use labels for Sex as recorded in the eCRF. Include Not Recorded rows if missing values are present.	SAC
1.10.	Enrolled	DM1	Summary of Demographic Characteristics	Note: This is a placeholder. Only to be created when Enrolled Population is different from All Treated Population. If this table is required, repeat all notes as above table.	SAC

1.11.	Enrolled	DM11	Summary of Age Ranges	Add a total column (total over all participants from both Part 1A and 2A).	SAC
Disease Characteristics					
1.12.	All Treated	DC_S1	Summary of Disease Characteristics at Initial Diagnosis	Cannot include head and neck cancer type as this information is not captured in the eCRF. Cannot include stage as stage was only recorded at screening (not at initial diagnosis). Histology and Histological grade options come from eCRF. Include Primary Tumor HPV Status and Primary Tumor MSI Status.	SAC
1.13.	All Treated	DC_S2	Summary of Disease Characteristics at Study Screening	Add “Measurable Disease at Screening”, “Time Since Last Progression (days)”, “Metastatic Disease at Screening” and “Time to Metastatic Disease (days)”. Include “Not Recorded” row if missing values are present for stage. Cannot include the following rows from the standard as the data were not collected in the eCRF: visceral and/or non-visceral disease, disease type and time since diagnosis of locally advanced disease. “Time Since Diagnosis of …” is renamed “Time Since …” to match the eCRF. Also, in the standard, the “Time Since Diagnosis of…” metrics are only calculated for certain	SAC

				participants, depending on disease type. As disease type was not collected, these metrics will be calculated on all participants with available data. Recurrent Local Disease is renamed as "Last Recurrence" to match the eCRF. Add footnotes: [1] Reference date is first exposure date Footnote for Time to Metastatic Disease [2]: [2] Reference date is initial diagnosis date	
Anti-Cancer Therapy					
1.14.	All Treated	AC_S1	Summary of Anti-Cancer Therapy – Prior to Study Screening	Cannot include the following rows from the standard as the data were not collected in the eCRF: setting of line of therapy, reason for stopping this line of therapy, relapse details, time since progression/relapse, most recent response for last line of therapy, most recent/best biomarker response assay for last line of therapy and most recent/best biomarker response for last line of therapy. Include "Any prior checkpoint inhibitors". Rearrange the order of the questions so that any prior checkpoint inhibitors is second, intent for line of therapy is third and the subsequent questions remain in their current order.	SAC

				Categories for prior line of therapy: 1, 2, 3, 4, >=5. Units for duration of lines of therapy: weeks. Add in footnotes: "Note: Only anti-cancer systemic therapy, as adjudicated by the clinical team, and cancer related surgical/medical procedures, as classified by the investigator on the eCRF, are included in the display." "Note: Anti-cancer therapies starting before the first dose of study intervention are included in the display." Footnote [1] added to number of prior lines of anti-cancer therapy, duration of line of therapy and best response for last line of therapy. "[1] Only anti-cancer therapies with advanced or metastatic intent are included."	
1.15.	All Treated	AC_S2	Summary of Anti-Cancer Radiotherapy - Prior to Study Screening	Cannot include the following rows from the standard as the data were not collected in the eCRF: setting and number of fractions (all units). In the standard, the types of radiotherapy are reported under “Any prior radiotherapy” – this level of detail in not collected in this study and so the options are “Yes” and “No”.	SAC

				Add footnote: "Note: Radiotherapies starting before the first dose of study intervention are included in the display."	
Crossover					
1.16.	All treated	POP_T1	Summary of Part 1A Subjects who Crossed Over to a Combination Therapy	Non-standard table. Use mock shell POP_T1. Include dose levels from Part 1A only.	SAC

12.10.5. Safety Tables

For all relevant tables, add the footnote: "Note: Subjects with Uncoded Adverse Events have not been included." when there are uncoded AEs.

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	All Treated	AE13	Summary of All Treatment-Emergent Adverse Events Overview	Include crossover cohorts.	SAC
3.2.	All Treated	AE5B	Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and Maximum Grade	Include crossover cohorts. Add footnote: “Note: The table represents the number of participants in each category.”	IB, SAC
3.3.	All Treated	AE5B	Summary of Drug-Related Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade	Include crossover cohorts.	SAC
3.4.	All Treated	AE3	Summary of Drug-Related Treatment-Emergent Adverse Events by Preferred Term	Include crossover cohorts. Add footnote: “Note: The table represents the number of participants in each category.” Add footnote “Note: The table is sorted by decreasing total frequency, where the total is calculated using all parts (Part 1A, Part 2A and Crossover).”	IB, SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.5.	All Treated	AE15	Summary of Common (>=5%) Non-serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	Include crossover cohorts. Update text to say TEAE instead of AE.	SAC
3.6.	All Treated	AE3	Summary of Common (>=10%) Treatment-Emergent Adverse Events by Overall Frequency	Include crossover cohorts. Add footnote: “Note: The table represents the number of participants in each category.” Add footnote: “Note: TEAEs are included in the table if they were experienced by either >=10% of participants in Part 1A OR >=10% of participants in the combined total from Part 2A and the Crossover cohorts.” Add footnote: “Note: The table is sorted by decreasing total frequency, where the total is calculated using all parts (Part 1A, Part 2A and Crossover).”	IB, SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.7.	All Treated	AE3	Summary of Non-Serious Drug-Related Treatment-Emergent Adverse Events by Overall Frequency	Include crossover cohorts. Add footnote: “Note: The table represents the number of participants in each category.” Add footnote: “Note: The table is sorted by decreasing total frequency, where the total is calculated using all parts (Part 1A, Part 2A and Crossover).”	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events of Special Interest					
3.8.	All Treated	AE5B_SI	Summary of Treatment-Emergent Adverse Events of Special Interest by Category, Preferred Term and Maximum Toxicity Grade	Categories: Cytokine Release Syndrome Event/Infusion Related Reaction [1], Immune-related Event [2] Include crossover cohorts. Add the footnotes: Note: The table represents the number of participants in each category. [1] TEAEs are included if they satisfy one of the following three criteria: (a) The site indicated the AE is a CRS event on the eCRF; (b) The decoded AE term is “Cytokine Release Syndrome”; (c) The decoded AE term is “Infusion Related Reaction” AND the site did not indicate that the AE is an immune-related event on the eCRF [2] TEAEs are included if the site indicated the AE is an immune-related event on the eCRF.	IB, SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.9.	All Treated	SAFE_T3	Summary of Treatment-Emergent Cytokine Release Syndrome Adverse Events and Infusion Related Reactions (Number of Participants and Occurrences)	Non-standard table, see mock shell. Include crossover cohorts. Only include TEAES that were MedDRA coded as "Cytokine release syndrome" or "Infusion Related Reaction". See mock shell for footnotes.	IB, SAC
Serious Adverse Events (SAEs)					
3.10.	All Treated	AE16	Summary of Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences)	Include crossover cohorts. Update text to say treatment emergent SAEs instead of SAEs.	SAC
3.11.	All Treated	AE20	Summary of Serious Fatal and Non-Fatal Drug-Related Treatment-Emergent Adverse Events by Overall Frequency	Include crossover cohorts.	SAC
3.12.	All Treated	AE5B	Summary of Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and Maximum Grade	Include crossover cohorts.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.13.	All Treated	AE3	Summary of Serious Treatment-Emergent Adverse Events by Preferred Term	Include crossover cohorts. Add footnote: Note: The table represents the number of participants in each category. Add footnote "Note: The table is sorted by decreasing total frequency, where the total is calculated using all parts (Part 1A, Part 2A and Crossover)."	IB, SAC
3.14.	DLT Evaluable	SAFE_T1	Summary of Number of DLTs, AEs, SAEs for all subjects	Events include Dose Limiting Toxicities (DLTs), SAEs related to treatment, SAEs not related to treatment, Grade 3 non-serious AEs related to treatment, Grade 3 non-serious AEs not related to treatment	DEM
3.15.	DLT Evaluable	SAFE_T2	Summary of Number of Events and Subjects by Maximum Grade	Events include Cytokine Release Syndrome, Hypoxia, Hypotension/Decreased Blood Pressure, Fever	DEM

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.16.	DLT Evaluable	AE19	Summary of Dose-Limiting Toxicities (DLT) During the Determinative Period	Include footnote: Note: DLT Rate = (No. of Subjects with DLT/No. of Subjects Evaluable for DLT) * 100. Note: Part 1A (excluding the Japan cohort) will be limited to participants with a screening visit before 01JAN2022. CCI [redacted]	IB, SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Deaths					
3.17.	All Treated	DD1	Summary of Deaths	Add footnotes: Note, participants who cross over are included in their monotherapy cohort. "[1] Last dose of any study treatment: initial treatment if the participant did not cross over or combination therapy if the participant did cross over."	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Hepatobiliary (Liver)					
3.18.	All Treated	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities	Include crossover cohorts. Rename "Hepatocellular injury" as "((ALT/ALT ULN)/(ALP/ALP ULN)) > 5 and ALT >3xULN". Re-label footnote [5] from the standard to "[5] ALT and ALP values must occur on the same day." Add footnote: "Note: n is the number of participants with at least one post-baseline lab chemistry measurement for the specified lab test(s)".	SAC
Exposure					
3.19.	All Treated	EX5	Summary of Exposure to GSK3745417 During Each Period	Dose intensity has units "mg/cycle". Modify footnote to: [1] Dose intensity is the cumulative actual dose divided by the number of cycles. Include the crossover cohorts.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.20.	All Treated	EX5_1	Summary of Exposure to GSK3745417 Across All Periods	Dose intensity has units “mg/cycle”. Modify footnote to: [1] Dose intensity is the cumulative actual dose divided by the number of cycles. Include the crossover information but display the information in the original monotherapy cohorts. Add the footnote: “Note: the display includes all exposure data from first GSK3745417 infusion to last GSK3745417 infusion, regardless of whether participants in the monotherapy cohorts later crossed over to combination cohorts. All information is displayed in the originally assigned cohort.”	SAC
3.21.	All Treated	EX5_2	Summary of Exposure to Dostarlimab	Include dose levels from Part 2A only and the crossover cohorts. Dose intensity has units “mg/cycle”. Modify footnote to: [1] Dose intensity is the cumulative actual dose divided by the number of cycles.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Dose Modifications					
3.22.	All Treated	OEX9	Summary Listing of Overall Exposure and Dose Modifications	Include GSK3745417 as component for all Part 1A dose levels/regimens and both GSK3745417 and Dostarlimab for all Part 2A dose levels/regimens. Interruptions should be labelled as “Infusion Interruptions”. If a participant crosses over to combination therapy, then all dose exposure and modifications from both the monotherapy and combination periods will be included in a single GSK3745417 component row. Modify footnote to: [1] Dose intensity is the cumulative actual dose divided by the number of cycles.	SAC

12.10.6. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK					
4.1.	Pharmacokinetic	PK01	Summary of GSK3745417 Plasma Concentration Time Data	Include crossover cohorts. Include the footnotes: Note: Participants are grouped by actual dose received at each respective visit and their originally assigned regimen schedule (Q1W or Q3W). (Only add if little n is greater than N at least once) Note: n (# of participants with a non-missing value used in analysis) may be greater than N (# of participants in cohort) if participant received different dose from initially assigned dose at a visit. Note: If more than 30% of values at a timepoint are imputed, then StD will not be displayed. Note: No. Imputed = Number of subjects who had concentration below Lower Limit of Quantification (LLQ) and concentration value imputed to zero. Note: 3 assays were used in this study, the corresponding LLQ values were: 0.005 ng/mL, 5 ng/mL and 0.1 ng/mL. Please see corresponding listing	SAC

Pharmacokinetic: Tables					
				for which LLQ was used for a particular sample.	
4.2	Pharmacokinetic	PK06	Summary of Derived GSK3745417 Plasma PK Parameters (non-transformed and log-transformed)	Include crossover cohorts. Parameters are provided in Table 3. Include the footnotes: Note: Participants are grouped by actual dose received at each respective visit and their originally assigned regimen schedule (Q1W or Q3W). (Only add if little n is greater than N at least once) Note: n (# of participants with a non-missing value used in analysis) may be greater than N (# of participants in cohort) if participant received different dose from initially assigned dose at a visit.	SAC

12.10.7. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK					
4.1	Pharmacokinetic	PK16A	Individual GSK3745417 Plasma Concentration -Time Plots (Linear and Semi-Log)	Include crossover cohorts, if feasible with space. Only include selected visits due to space on the legend (this may mean crossover cohorts are not included). Use same footnote as Table 4.1 regarding LLQ.	SAC
4.2 4.3 4.4	Pharmacokinetic	PK17	Mean (+SD) GSK3745417 Concentration-Time Plots (Linear and Semi-log)	Include crossover cohorts. Include the footnotes: XO = Crossover cohort. All cohorts for this dose are included in the legend, but the cohorts will only appear on the figure if a sample was collected for that visit (e.g. the Q3W cohorts will only appear on the Week 1, 4, 7, and so on, figures). Note: Participants are grouped by actual dose received at each respective visit and their originally assigned regimen schedule (Q1W or Q3W).	SAC

Pharmacokinetic: Figures					
				Use same footnote as Table 4.1 regarding LLQ. The display will be split onto three figures, with the following cohorts included on each figure: CCI [redacted]	
4.5 4.6 4.7	Pharmacokinetic	PK18	Median GSK3745417 Concentration-Time Plots (Linear and Semi-log)	Include crossover cohorts. Include the footnotes: XO = Crossover cohort. All cohorts for this dose are included in the legend, but the cohorts will only appear on the figure if a sample was collected for that visit (e.g. the Q3W cohorts will only appear on the Week 1, 4, 7, and so on, figures). Note: Participants are grouped by actual dose received at each respective visit and their originally assigned regimen schedule (Q1W or Q3W). Use same footnote as Table 4.1 regarding LLQ.	SAC

Pharmacokinetic: Figures					
				The display will be split onto three figures, with the following cohorts included on each figure: CCI [redacted]	
4.8	Pharmacokinetic	PK29	Plot of Individual (+Geometric Mean and 95% CIs) Plasma Dose-Normalized AUC(0-inf) versus Dose	If AUC(0-inf) is not calculable for the majority of participants, then use AUC(0-t). The mean will be provided for each treatment group and the individual participant data will be plotted, for example, with a coded symbol. The 95% CIs will be provided for the treatment groups with at least three participants. Only selected visits may be included (this may mean crossover cohorts are not included as they are treated as separate visits). Add the footnote: Note: Participants are grouped by actual dose received at each respective visit and their originally assigned regimen schedule (Q1W or Q3W).	SAC
4.9	Pharmacokinetic	PK29	Plot of Individual (+Geometric Mean and 95% CIs) Plasma Dose-Normalized Cmax versus Dose	Use notes for the other PK29 figure including the additional footnote.	SAC

CCI

12.10.9. ICH Listings

Note, only static listings are given below.

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.	All Treated	ES2	Listing of Reasons for Study Withdrawal	Treatment assignment is as per original assignment (not crossover assignment). Include “Crossover” as a separate column with “Yes” and “No”. Add period day after study day (same column). Rename “Reason Term(s)” to “Reason Specify”. Include “Relationship to COVID-19” with “Not-Related”, “Related” and “Unknown”.	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.	All Treated	SD2xo	Listing of Reasons for Study Treatment Discontinuation from GSK3745417	For the second column: Treatment Sequence [1]/ Treatment/ Period. Treatment Sequence = M/MC/C. Period is Monotherapy or Combination. Add period day after study day (same column) for both instances. Rename “Reason Term(s)” to “Reason Specify”. Include “Relationship to COVID-19” with “Not-Related”, “Related” and “Unknown”. Add footnote: [1] M = Monotherapy only, MC = Monotherapy then Combination therapy (Crossover), C = Combination therapy only. Add footnote: Note: participants who crossover from monotherapy to combination therapy have two rows in the listing, one for their monotherapy and one for their combination therapy.	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.	All Treated	SD2	Listing of Reasons for Study Treatment Discontinuation from Dostarlimab	Include dose levels from Part 2A and the crossover cohorts only. Add period day after study day (same column) for both instances. Rename “Reason Term(s)” to “Reason Specify”. Include “Relationship to COVID-19” with “Not-Related”, “Related” and “Unknown”.	SAC
Protocol Deviations					
5.	All Treated	DV2	Listing of Important Protocol Deviations	Include “Relationship to COVID-19” with “Not-Related”, “Related” and “Unknown”. Include crossover cohorts. Add period day after study day (same column).	SAC
6.	All Treated	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Populations Analysed					
7.	Enrolled	SP3	Listing of Subjects Excluded from All Treated Population		SAC
Demographic and Baseline Characteristics					
8.	All Treated	DM2	Listing of Demographic Characteristics	Include Race.	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Prior and Concomitant Medications					
9.	All Treated	CM3	Listing of Concomitant Medications using Ingredient	Include crossover cohorts. Add period day after study day (same column) for start and stop. Do not include start and stop time as this information is not collected in the eCRF. Add footnote: "For crossover participants, where the start and/or end date of the concomitant medication was missing and the period of use could not be determined, the concomitant medication is included in both the monotherapy and crossover cohort"	SAC
Exposure and Treatment Compliance					
10.	All Treated/DLT Evaluable	OEX8C	Listing of Exposure to GSK3745417	Run the listing on DLT evaluable population for DEM; otherwise All Treated. Include rows for treatment received during the crossover period. Add period day after study day (same column) for start and stop.	DEM, SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
11.	All Treated/DLT Evaluable	OEX8B	Listing of Exposure to Dostarlimab	Run the listing on DLT evaluable population for DEM; otherwise All Treated. Include dose levels/regimens from Part 2A and crossover cohorts. Add period day after study day (same column) for start and stop.	DEM, SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
12.	All Treated/ DLT Evaluable	AE8	Listing of All Adverse Events	Run the listing on DLT evaluable population for DEM; otherwise All Treated Note: Include Dose-Limiting Toxicity information (DLT evaluable and DLT) for all deliverables. Include the crossover cohorts. Add “AE of special interest” with options "Immune-related event", "Cytokine Release Syndrome event" and missing. Add treatment emergent flag. Add footnote [1] after “Time Since 1st Dose”: “[1] For the crossover cohorts, time since first dose refers to the first monotherapy dose (not the first combination [crossover] dose).”	DEM, SAC
13.	All Treated/DLT Evaluable	AE8	Listing of Adverse Events Leading to Permanent Discontinuation of Study Treatment	Run the listing on DLT evaluable population for DEM; otherwise All Treated Include crossover cohorts. Add treatment emergent flag.	IB, DEM
14.	DLT Evaluable	AE8	Listing of Serious Adverse Events	Include crossover cohorts. Add treatment emergent flag.	DEM

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
15.	All Treated	AE8	Listing of Non-Fatal Serious Adverse Events	Include the crossover cohorts. Add treatment emergent flag.	IB
16.	All Treated	AE8	Listing of Grade 3 and 4 Adverse Events	Include the crossover cohorts. Add treatment emergent flag.	IB
17.	All Treated	AE14	Listing of Reasons for Considering as a Serious Adverse Event	Include the crossover cohorts. Include treatment emergent flag. Remove “Prot [7]” and footnote as this is not collected in the study.	SAC
18.	All Treated	AE8	Listing of IRR/CRS Related Adverse Events	Include the crossover cohorts. Add treatment emergent flag. Add the footnote: Note: AEs are included if they satisfy one of the following three criteria: (1) The site indicated the AE is a CRS event on the eCRF; (2) The decoded AE term is “Cytokine Release Syndrome”; (3) The decoded AE term is “Infusion Related Reaction”.	IB
19.	All Treated	AE8	Listing of Immune-related Adverse Events	Include the crossover cohorts. Add treatment emergent flag.	IB

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Deaths					
20.	All Treated	DD3	Subject Profile for Death	Treatment: This is the last treatment before death. For those who crossover, use the standard crossover cohort label. Treatment sequence: M / MC / C Period: Monotherapy / Combination Therapy. Add a footnote after “Treatment Sequence”: "[1] M = Monotherapy only, MC = Monotherapy then Combination therapy (Crossover), C = Combination therapy only." Add a footnote after "Start Date of Treatment": "[2] For participants who crossover from monotherapy to combination therapy (have treatment sequence MC) this is the start date of the monotherapy." Add a footnote after "End Date of Treatment”: "[3] For participants who crossover from monotherapy to combination therapy (have treatment sequence MC) this is the end date of the combination therapy."	IB, SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory					
21.	All Treated	LB5A	Listing of All Laboratory Data for Participants with Any Value Outside of Normal Range	Add change from baseline column. The NR flag column should be completed for baseline rows. Include the crossover cohorts. Add period day after study day (same column). Add footnote: "Note: if the upper and/or lower limit of the normal range is missing, then the NR flag and grade cannot be derived."	SAC
22.	DLT Evaluable	SAFE_L1	Listing of Grade>=3 Laboratory Data for CBC with Differential	Include tests Creatinine, ALT, AST, Total bilirubin, Direct bilirubin, eGFR, platelets, Haemoglobin, Total white cell count, Neutrophils, Lymphocytes, PT/INR.	DEM
23.	All Treated	UR2	Listing of Urinalysis Data for Subjects with Any Value of Potential Clinical Importance	Include the crossover cohorts. Add period day after study day (same column).	SAC

12.10.10. Non-ICH Listings

Note, only static listings are given below.

Non-ICH Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK					
24.	Pharmacokinetic	PK07	Listing of GSK3745417 Pharmacokinetic Concentration-Time Data	Include crossover cohorts. Add period day after study day (same column). Add PK analysis exclusion flag. Only if actual dose does not equal planned dose for at least one entry: Add the column "Actual Dose (mg) [1]" after Study Day. Include the footnote: "[1] Actual dose is only populated if it differs from the expected dose." Include the column "LLQ (ng/mL)" before concentration. This should be provided by the BIB data release for each sample (participant visit), depending on the assay used. If a value is NQ, it should be reported as "(NQ)" in the concentration column.	SAC

				Add footnote: "Note: 3 assays were used in this study, the corresponding LLQ values were: 0.005 ng/mL, 5 ng/mL and 0.1 ng/mL."	
25.	Pharmacokinetic	PK13	Listing of GSK3745417 Pharmacokinetic Parameters	Include crossover cohorts. Only if actual dose does not equal planned dose for at least one entry: Add the column "Actual Dose (mg) [1]" after Visit. Include the footnote: "[1] Actual dose is only populated if it differs from the expected dose." Parameters are provided in Table 3.	SAC