Statistical Analysis Plan (SAP)

Study ID: 213299

Official Title of Study: A Global, Molecular Disease Characterization Initiative (MDCI) in Oncology Clinical Trials

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TITLE PAGE

Protocol Title: A Global, Molecular Disease Characterization Initiative (MDCI) in Oncology Clinical Trials

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Version history

SAP Version	Approval Date	Protocol Version (Date) on which SAP is Based	Change	Rationale
1	29 Nov 2022	Amendment 03 (25-Oct-2021)	Not Applicable	Original version

1. INTRODUCTION

The purpose of this SAP is to describe the planned analyses to be included in the synoptic CSR and disclosure for Study 213299. Details of the planned analyses are provided.

1.1. Objectives, Estimands and Endpoints

Estimands are not applicable for this study.

1.1.1. Objectives and Endpoints

Objectives	Endpoints
Primary	
• To evaluate molecular and immunological profile of tumor and peripheral blood of all enrolled participants, across indications and within tumor subsets (Building a GSK Clinical Science Database for tumor profiling and correlative studies).	• Profile of patient specific selection biomarkers targeted by therapeutics with the GSK oncology pipeline, as well as other CCI as detailed in the study reference manual (SRM).
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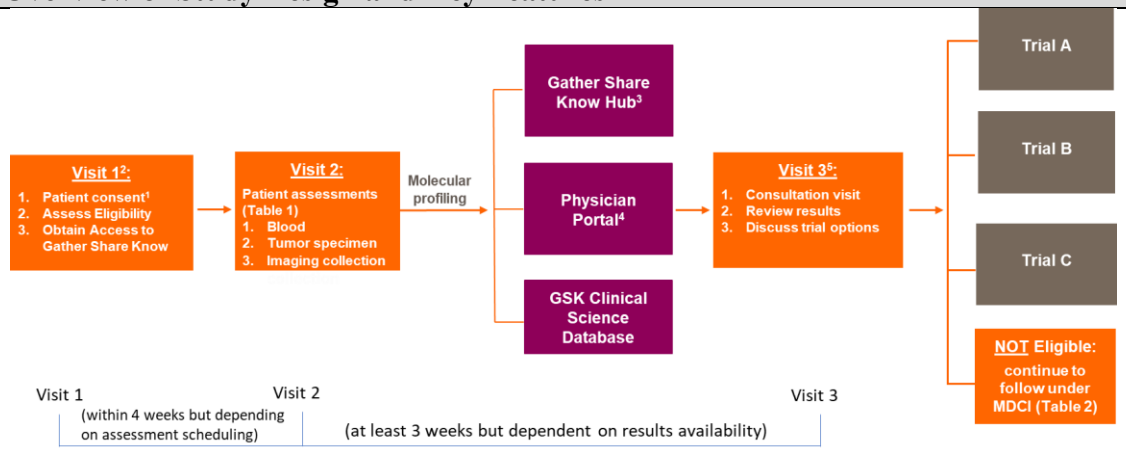
[redacted]

1.2. Study Design

Overview of Study Design and Key Features



Footnotes: [1]MDCI will be an optional protocol under select GSK oncology protocols; [2]In the case that Visit 1 and 2 are combined, all corresponding samples must be collected per the SoA (Protocol Section 1.3) at this visit and after eligibility is confirmed; [3]Subset of data to be shared on Gather Share Know; [4]Patient's molecular profile and medical history will be compared against the eligibility criteria of select GSK oncology protocols to identify potential trial options; [5]Visit 3 may occur remotely via

Overview of Study Design and Key Features	
telehealth/phone visit. Table 1 & 2 referenced in the study schema are located in the protocol amendment 3.	
Design Features	This is a multicenter study, enrolling participants with advanced/metastatic disease for the purpose of biospecimen collection (tumor tissue and blood samples) for broad molecular profiling and examining the expression of specific antigens (e.g. NY-ESO-1, LAGE-1a), immune markers (e.g. PD-L1), tumor immune infiltrates, differentially expressed genes, and Human Leukocyte Antigen (HLA) genotype. Results from validated clinical assays will support the referral of eligible participants into an appropriate GSK Clinical trial. This study will include three visits: At **Visit 1**, informed consent will be obtained from participants to enroll in the study, specifically to undergo a multiplex CCI characterization, and to store and share a subset of their data through a Participant Hub (Gather Share Know). During **Visit 2**, a tumor specimen will be collected or submitted, as per tumor specimen collection requirements (refer to SRM and Study Laboratory Manual). The specimen will be evaluated by IHC to determine the expression of tumor specific antigens and immune markers such as, but not limited to, NY-ESO-1 and PD-L1. A liquid biopsy (blood) will also be taken at Visit 2 to analyse CCI CCI circulating tumor DNA (ctDNA), CCI CCI, and/or exosomes. In addition, participants will also provide mandatory blood samples for CCI, validated clinical CCI testing, and genetic research, as well as tumor imaging with CT/MRI. Following the Visit 2, a subset of the generated results will be uploaded to the Physician Portal for review, followed by the Gather Share Know Participant Hub. Physicians will review the results with participants at **Visit 3**.

Overview of Study Design and Key Features	
Study intervention	Not applicable
Study intervention Assignment	Not applicable
Interim Analysis	Due to the continuous nature of this study, there is no interim analysis phase.

2. STATISTICAL HYPOTHESES

MDCI is an CCI [redacted] study and a pre-screening protocol. The analysis will be descriptive in nature. No formal hypothesis testing is planned under this study.

2.1. Multiplicity Adjustment

No formal statistical testing will be performed; therefore, no adjustments for multiplicity are planned.

3. ANALYSIS SETS

Analysis Set	Definition / Criteria	Analyses Evaluated
Screened	• All participants who sign the ICF	• Study population
Enrolled	• All participants who sign the ICF and meet inclusion/exclusion criteria	• Study Population • Safety

4. STATISTICAL ANALYSES

4.1. General Considerations

Unless and otherwise specified, only the study column will be reported in summary tables.

4.1.1. General Methodology

Unless otherwise specified, continuous data will be summarized using descriptive statistics: n, mean, standard deviation (std), median, minimum and maximum. Categorical data will be summarized as the number and percentage of participants in each category.

It is anticipated that patient accrual will be spread thinly across centres and summaries of data by centre would unlikely be informative and will not, therefore, be provided.

4.1.2. Baseline Definition

No endpoints/summary measures are reported which requires baseline definition. Hence, not applicable.

4.2. Primary Endpoint(s) Analyses

4.2.1. Definition of endpoint

Profile of patient-specific selection biomarkers that are targeted by therapeutics within the GSK oncology pipeline, as well as other CCI as detailed in the study reference manual (SRM).

4.2.2. Main analytical approach

"Enrolled" analysis set will be used to perform primary endpoint analysis.

A summary table containing biomarker status of participants will be provided. Biomarker status includes Inducible T-cell Co-Stimulator (ICOS) status, New York esophageal squamous cell carcinoma 1 (NY-ESO-1)/Cancer testis antigen 2 (LAGE-1a) status and Programmed death protein 1 Ligand (PD-L1) status.

This summary table contains number and percentage of participants with positive/negative status by biomarker (ICOS, NY-ESO-1/LAGE-1a and PD-L1).

A subject level listing containing biomarker status of participants will also be provided.

4.3. Secondary Endpoint(s) Analyses

Not applicable, as there are no secondary endpoints defined under this protocol.

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4.5. Safety Analyses

The safety analyses will be based on the Enrolled Analysis Set, unless otherwise specified.

Only the AEs/SAEs related to study procedures are collected in this study. If there are no AEs/SAEs in the database, a standard 'No data to report' display will be generated.

4.5.1. Extent of Exposure

Not applicable.

4.5.2. Adverse Events/Serious Adverse Events

Adverse events analyses including the analysis of adverse events (AEs), serious adverse events (SAEs) will be based on GSK Core Data Standards. Adverse events will be coded using the standard Medical Dictionary for Regulatory Affairs (MedDRA dictionary) and grouped by system organ class (SOC). Adverse events will be graded by the investigator according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE v5.0).

An overview summary of AEs, including counts and percentages of participants with any AE will be created by SOC and PT.

All SAEs will be tabulated based on the number and percentage of participants who experienced the event by SOC and PT. The summary of all SAEs will be created by SOC and PT.
A summary of fatal SAEs will also be provided.

A Summary of Fatal AEs and Non-serious AEs by SOC and PT will also be provided.

A listing of all AEs collected will be provided. SAE flags are included in the listing of all AEs. Separate supportive listings with participant level details will be generated for

- Fatal SAEs
- Non-Fatal SAEs.

4.5.2.1. Additional Safety Assessments

Routine safety assessments (e.g., ECG and vital signs) were only collected during screening. Other than the collection of AE information, no further safety assessments were mandated in the protocol after screening was complete. Therefore, no additional safety information will be summarised for this study.

4.6. Interim Analyses

Due to the continuous nature of this study, there is no interim analysis phase. Data will be continuously monitored and analysed in real-time during the course of the study.

4.7. Changes to Protocol Defined Analyses

There were no changes or deviations to the originally planned statistical analysis specified in the protocol amendment 3 (Dated: 25-OCT-2021).

5. SAMPLE SIZE DETERMINATION

Since MDCI does not aim to test any specific hypothesis or answer any particular question, there is no statistical requirement to reach a specific number of samples and patients.

6. SUPPORTING DOCUMENTATION

6.1. Appendix 1 Study Population Analyses

Unless otherwise specified, the study population analyses will be based on the Enrolled Analysis Set.

6.1.1. Participant Disposition

A summary of the number of participants in each of the participant level analysis set mentioned in Section 3 will be provided.

A summary of subject status and reason for study withdrawal will be provided. This display will show the number and percentage of subjects who withdrew from the study, including primary reasons for study withdrawal. The Enrolled Analysis set will be used.

A summary and listing of screening status and reasons for screen failure will be provided using the Screened Analysis Set. Per GSK reporting standards, participants who were rescreened will appear once in these displays according to their final status.

6.1.2. Demographic and Baseline Characteristics

The demographic characteristics including age, gender, ethnicity, weight at screening and race will be summarized with descriptive statistics. In addition, the following age categories will be summarized: 18-64, 65-84 and >=85 based on the Enrolled Analysis Set.

A listing of demographic characteristics and race will be provided.

6.1.3. Protocol Deviations

Important protocol deviations will be summarized.

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 (where possible without knowing the study intervention details) are captured and categorised in the protocol deviations dataset.
- This dataset will be the basis for the summaries of important protocol deviations.

If there is no data to report a standard “no data to report” displays will be produced.

6.2. Appendix 2 Data Derivations Rule

6.2.1. Study Day and Reference Dates

The reference date is the study enrolment date and will be used to calculate study day

The study day is calculated as below:

- Assessment Date = Missing → Study Day = Missing
- Assessment Date < Reference Date → Study Day = Assessment Date – Ref Date
- Assessment Data ≥ Reference Date → Study Day = Assessment Date – Ref Date + 1

6.2.2. Assessment Window

No Assessment window will be applied.

6.2.3. Handling of Partial Dates

The partial date imputation will follow ADaM conventions. The ADaM approach is to populate the numeric date variables with the imputed date and add a flag variable to the dataset that indicates the level of imputation.

The flag variable can contain the values: blank, 'D', 'M', 'Y'.

blank: indicates that no imputation was done

D='Day': indicates that the day portion of the date is imputed

M='Month': indicates that the month and day portions of the date are imputed

Y='Year': indicates that the entire date (year, month, and day) is imputed

Example of date variables:

XYZD_ - character date variable

XYZDT - numeric date variable

XYZDTFL - flag variable

Details on imputing partial dates for specific datasets are outlined below

<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
<tr><td>General</td><td>

Partial dates will be displayed as captured in participant listing displays.
However, where necessary, display macros may impute dates as temporary variables for sorting data in listings only. In addition, partial dates may be imputed for ‘slotting’ data to study phases or for specific analysis purposes as outlined below.
Imputed partial dates will not be used to derive study day, time to onset or duration (e.g., time to onset or duration of adverse events), or elapsed time variables (e.g., time since diagnosis).

</td></tr>
<tr><td>Adverse Events</td><td>

Partial dates for AE recorded in the CRF will be imputed using the following conventions:

<table>
<tr><td>Missing start day</td><td>If study enrollment date is missing, then set start date = 1st of month.

Else if study enrollment date is not missing:

o If month and year of start date = month and year of study enrollment date, then

▪ If stop date contains a full date and stop date is earlier than enrollment date, then set start date= 1st of month.

▪ Else set start date = study enrollment date.

Else set start date = 1st of month.</td></tr>
<tr><td>Missing start day and month</td><td>If study enrollment date is missing, then set start date = January 1.

Else if study enrollment date is not missing:

o If year of start date = year of enrollment start date, then

▪ If stop date contains a full date and stop date is earlier than study enrollment date, then set start date = January 1.
▪ Else set start date = study enrollment date.
Else set start date = January 1.</td></tr>
</table>
</td></tr>
</table>

Element	Reporting Detail	
	Missing end day	A '28/29/30/31' will be used for the day (dependent on the month and year).
	Missing end day and month	No Imputation
	Completely missing start/end date	No imputation

6.2.4. Early PK Access Key Activities

Not applicable.

7. REFERENCES

None