Information Type:	Statistical Analysis Plan (SAP)

TITLE PAGE

Protocol Title: A Screening Protocol to Support Preliminary Eligibility for Clinical Trials Evaluating Safety and Efficacy of Adoptive Cell Therapies in Participants with Solid Tumors and Hematologic Malignancies.

Study Number: 213033

Compound Number: Not Applicable

Abbreviated Title: Screening Protocol for Preliminary Eligibility Determination for Adoptive Cell Therapy Trials

Sponsor Name: GlaxoSmithKline Research & Development Limited

Regulatory Agency Identifier Number(s)

Registry	**ID**
	NA

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Version history

SAP Version	Approval Date	Protocol Version (Date) on which SAP is Based	Change	Rationale
1.0	28 Nov 2022	22-JUN-2021	Not Applicable	Original version

1. INTRODUCTION

The purpose of this SAP is to describe the planned final analyses for Study 213033. Due to the lack of enrolment and poor site engagement, the study has been terminated early. The analyses specified in this plan is to support the synoptic CSR only.

1.1. Objectives, Estimands and Endpoints

Estimands are not applicable for this study.

Objectives	Endpoints
Primary (Operational)	
• Determine germline HLA genotype of all enrolled participants.	• Prevalence of HLA-A*02:01, HLAA* 02:05, or HLA-A*02:06 allele subtypes
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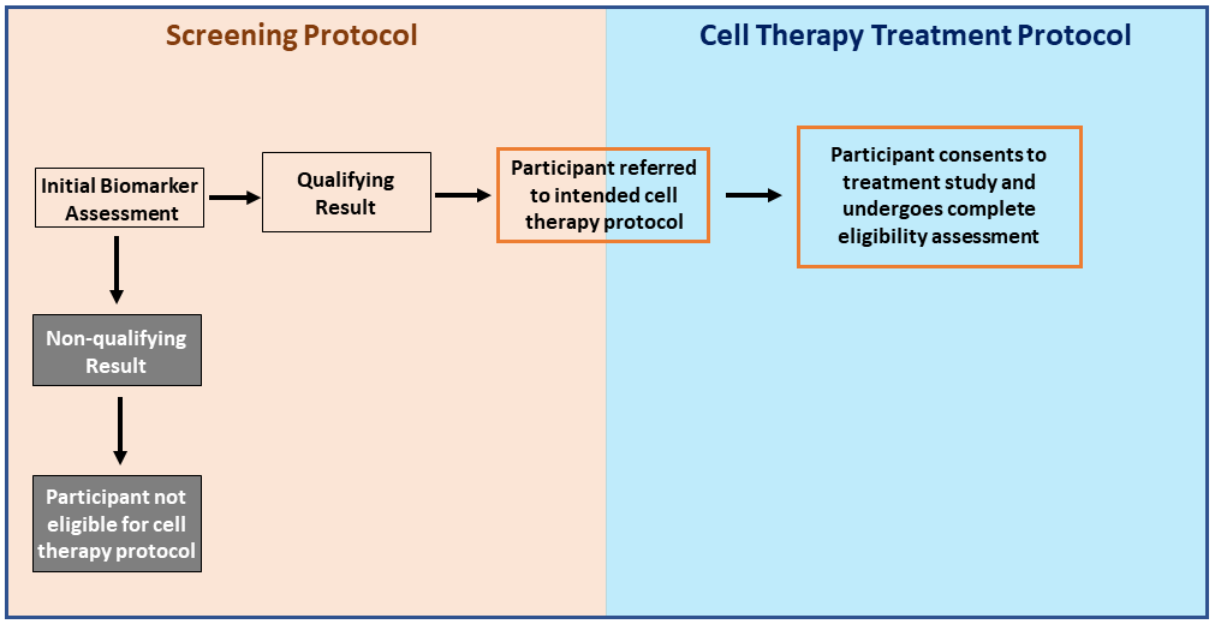
[1] MRCLS: Myxoid/round cell liposarcoma

1.2. Study Design

Overview of Study Design and Key Features



Design Features	· This multicenter screening study will assess initial biomarker status to facilitate referral of eligible patients for further evaluation to a GSK cell therapy trial site enrolling participant with various malignancies · This screening protocol will support clinical trials of lete-cel, GSK3901961 & GSK3845097, in tumor types currently under investigation as well as additional indications and other GSK cell therapy assets in the future · During study Visit 1, all participants who consent to the screening study and are determined to meet the eligibility criteria for Study 213033 will provide the mandatory screening samples · If the participant is determined to have qualifying results for an intended investigational treatment protocol, then the participant may be considered for referral to GSK trial site to complete the rest of the eligibility assessments for the investigational treatment trial.
Study intervention	Not Applicable
Study intervention Assignment	Not Applicable
Interim Analysis	No interim analysis is planned for this study

2. STATISTICAL HYPOTHESES

This is a screening protocol. The analysis will be descriptive in nature. No formal hypothesis will be tested under this protocol.

2.1. Multiplicity Adjustment

No formal statistical testing will be performed; therefore, no adjustments for multiple comparisons or 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 provide sample for biomarker assessment	• Study Population • Safety

4. STATISTICAL ANALYSES

4.1. General Considerations

Unless and otherwise specified, indications tumour type will be used as table columns. Total column will be reported if more than one indication is reported.

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.

4.1.2. Baseline Definition

Unless and otherwise specified visit 1 assessments (screening visit) will be considered as baseline for demographics displays.

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

4.2. Primary Endpoint(s) Analyses

4.2.1. Definition of endpoint(s)

Prevalence of HLA-A*02:01, HLAA* 02:05, or HLA-A*02:06 allele subtypes.

4.2.2. Main analytical approach

“Enrolled” analysis set will be used to perform primary endpoint analysis.

A summary of participant’s HLA A genotype status will be provided. This summary contains the number and percentage of participants in each of the allele sub-types (HLA A genotypes).

A subject level listing containing allele subtypes and tumour types will also be provided.

4.3. Secondary Endpoint(s) Analyses

There are no secondary endpoints defined under this protocol. Hence, this section is not applicable.

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4.5. Safety Analyses

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

Only AEs which lead to study withdrawal, as determined, and collected in eCRF by the investigator 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) and preferred term (PT). Adverse events will be graded by the investigator according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE v 5.0).

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 Non-serious AEs and Fatal SAEs will also be provided by SOC and PT.

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.

4.5.3. Additional Safety Assessments

Since there is no Investigational Product administered in this study no laboratory parameters, vital signs and ECG data are collected; consequently, these safety assessments are not applicable.

4.5.3.1. Deaths

A subject level listing of deaths will be provided.

4.6. Interim Analyses

No interim analysis is planned for this study.

4.7. Changes to Protocol Defined Analyses

There were no changes or deviations to the originally planned statistical analysis specified in the protocol (Dated: 22-JUN-2021).

5. SAMPLE SIZE DETERMINATION

Approximately 1000 participants were planned to be enrolled in this screening study. However, the study has been closed early with limited enrolment.

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 analysis populations described in Section 3 will be provided. This summary also includes reasons for screen failure. A listing of participants from screened set but excluded from enrolled set will also be provided along with reason.

Study disposition will be provided for the "Enrolled" population if any subject withdraws from study.

A listing of screening status and screen failures 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.

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6.1.3. Protocol Deviations

Important protocol deviations will be listed.

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.
- Protocol deviations which result in exclusion from the analysis set will also be summarized. Data will be reviewed prior to freezing the database to ensure all deviations leading to analysis population exclusions are captured and categorised in the protocol deviations ADaM dataset (note these exclusions are not captured in the SDTM dataset).

6.1.4. Prior and Concomitant Medications

Not applicable.

6.2. Appendix 2 Data Derivations Rule

6.2.1. Criteria for Potential Clinical Importance

Not Applicable

6.2.2. 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*

6.2.3. Assessment Window

No Assessment window will be applied.

6.2.4. Multiple measurements at One Analysis Time Point

Not Applicable

6.2.5. 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

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays. • However, where necessary, display macros may impute dates as temporary variables for sorting data in listings only. In addition, partial dates may be imputed for 'slotting' data to study phases or for specific analysis purposes as outlined below. • Imputed partial dates will not be used to derive study day, time to onset or duration (e.g., time to onset or duration of adverse events), or elapsed time variables (e.g., time since diagnosis). In addition, imputed dates are not used for deriving the last contact date in overall survival analysis dataset.
Age	• If the month and day is missing, set to 30th of June

<table>
<tr><th>Element</th><th>Reporting Detail</th></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 enrolment date is missing, then set start date = 1st of month.

Else if study enrolment date is not missing:

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

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

▪ Else set start date = study enrolment date.

Else set start date = 1st of month.</td></tr>
<tr><td>Missing start day and month</td><td>If study enrolment date is missing (i.e. participant did not start study intervention), then set start date = January 1.

Else if study enrolment date is not missing:

o If year of start date = year of study enrolment date, then

▪ If stop date contains a full date and stop date is earlier than study enrolment date, then set start date = January 1.
▪ Else set start date = study enrolment date.
Else set start date = January 1.</td></tr>
<tr><td>Missing end day</td><td>A '28/29/30/31' will be used for the day (dependent on the month and year).</td></tr>
<tr><td>Missing end day and month</td><td>No Imputation</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table>
</td></tr>
</table>

6.2.6. Early PK Access Key Activities

Not Applicable

7. REFERENCES

None