Statistical Analysis Plan

Study ID: 219239

Official Title of Study: A Phase 1, randomized, open-label, parallel group study to evaluate the relative bioavailability of subcutaneous bepirovirsen when delivered from a vial or prefilled syringe fitted with a safety syringe device in healthy adult participants.

NCT ID: NCT06058390

Date of Document: 28-Aug-2023

NOTE: Please note that the first page of this document contains a dummy NCT ID which is redacted. For all references and purposes, the NCT ID mentioned above on this cover page is the correct and official identifier for this study.

Information Type:	Statistical Analysis Plan (SAP)

TITLE PAGE

Protocol Title: A Phase 1, randomized, open-label, parallel group study to evaluate the relative bioavailability of subcutaneous bepirovirsen when delivered from a vial or prefilled syringe fitted with a safety syringe device in healthy adult participants.

Study Number: 219239

Compound Number: GSK3228836

Abbreviated Title: A study to evaluate the relative bioavailability of subcutaneous bepirovirsen when delivered from a vial or prefilled syringe fitted with a safety syringe device in healthy adult participants.

[Acronym:]

Sponsor Name: GSK Research & Development Limited

Regulatory Agency Identifier Number(s)

Registry	**ID**
Clintrials.gov	[redacted]

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VERSION HISTORY

SAP Version	Approval Date	Protocol Version (Date) on which SAP is Based	Change	Rationale
SAP	28 Aug 2023		Not Applicable	Original version

1. INTRODUCTION

The purpose of this Statistical Analysis Plan (SAP) is to describe the planned analyses to be included in the CSR for Study 219239.

Descriptive study population analyses such as summary of demography and baseline characteristics and additional detail with regards to data handling conventions and the specification of data displays will be provided in the Output and Programming Specification (OPS) document.

1.1. Objectives, Estimands and Endpoints

Objectives	Endpoints
Primary	
• To estimate the relative bioavailability of vial and PFS SSD for a single dose of bepirovirsen delivered by SC injection by an HCP in healthy participants	• Cmax and AUC(0-inf) of bepirovirsen in plasma.
Secondary	
• To estimate the relative bioavailability of HCP administered vs self-administration following HCP training for a single dose of bepirovirsen delivered by SC injection in healthy participants	• Cmax and AUC(0-inf) of bepirovirsen in plasma.
• To estimate the relative bioavailability of HCP administered vs self-administration with no HCP training for a single dose of bepirovirsen delivered by SC injection in healthy participants	• Cmax and AUC(0-inf) of bepirovirsen in plasma.

Safety	
• To compare the safety and tolerability of CCI of bepirovirsen CCI mg by randomised group.	• Occurrences of AEs and SAEs • Change from baseline at each time point in clinical laboratory tests and vital signs
Exploratory	
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[redacted]

1.2. Study Design

Overview of Study Design and Key Features	
Design Features	This is a Phase 1, open-label, randomized study to investigate SC bepirovirsen when delivered via SC injection from a vial and PFS SSD in healthy adult participants. The study will assess relative bioavailability, safety, and tolerability, as well as the usability of the PFS SSD for self-administration. A total of approximately CCI participants will each complete a single study session, in a parallel design, and will take up to CCI weeks to complete the study. Participants will be screened within 28 days before dosing. They will attend the clinical unit the day before dosing (Day -1) and will remain inpatient until 2 days after dosing (Day 3). Participants will return for outpatient visits on Days CCI Blood samples will be taken to measure levels of bepirovirsen and ADAs against bepirovirsen, and safety and tolerability will be assessed from before dosing and until the final visit. The observing HCP and participants in Groups 3 and 4 will complete questionnaires, respectively, during and after dosing, to assess usability of the PFS SSD for self-administration. Blood samples will also be taken for biomarker analysis before dosing and up to 48h after dosing.
Study intervention	CCI [redacted]

Overview of Study Design and Key Features	
	CCI [redacted]
Study intervention Assignment	Participants will be randomized in a ratio of 3:3:2:2 to one of the four treatment groups. The randomization will be stratified by body weight (CCI [redacted]). The site of injection will be randomized in a 1:1:1 ratio to upper arm, abdomen, and thigh in Groups 1 and 2, and in a 1:1 ratio to abdomen or thigh in Groups 3 and 4.
Interim Analysis	CCI [redacted]

2. STATISTICAL HYPOTHESES

This study is designed to estimate the relative bioavailability of a CCI [redacted] of bepirovirsen administered SC from vial and PFS SSD presentations by a healthcare provider (HCP) in healthy participants. For Cmax and AUC(0-inf), point estimates and corresponding two-sided 90% CIs will be constructed for the ratio of the geometric mean of the vial to the PFS SSD.

An additional assessment will be conducted comparing the CCI [redacted] reference range of 0.8 to CCI [redacted]

2.1. Multiplicity Adjustment

No multiplicity adjustment will be implemented because the primary objective is to estimate the relative bioavailability of a CCI [redacted] of bepirovirsen, and no formal hypotheses will be tested.

3. ANALYSIS SETS

Analysis Set	Definition / Criteria	Analyses Evaluated
Screened	• All participants who were screened for eligibility.	• Study Population
Enrolled	• All participants who entered the study (who were randomized or received study intervention or underwent a post-screening procedure). • NOTE: screening failures (who never passed screening even if rescreened) and participants screened but never enrolled into the study (Met eligibility but not needed) are excluded from the Enrolled Analysis set as they did not enter the study.	• Study Population
Randomised	• All participants who were randomly assigned to study intervention in the study.	• Study Population
Safety	• Participants who received study intervention • Participants will be analysed according to the study intervention administered.	• Safety
PK concentration	• All participants in the Safety analysis who received CCI the injections and had at least 1 non-missing PK assessment (NQ values will be considered as non-missing values. • Data will be reported according to the actual study intervention.	• PK concentration
PK Parameter	• All participants in the PK concentration population for whom valid and evaluable plasma PK parameters are derived. This primary analysis population will be used in the assessment and characterization of PK parameters (summary and analysis tables and figures).	• PK parameter

4. STATISTICAL ANALYSES

4.1. General Considerations

4.1.1. General Methodology

The Safety analysis set will be used for all study population analyses and safety analyses, unless otherwise specified. The PK analysis set will be used for PK analyses. Study population and safety tables will be displayed overall and by randomised groups.

Any subjects randomised in error to the incorrect weight strata will be summarised based on the actual stratum per data collected in the CRF.

Confidence intervals will use 90% confidence levels unless otherwise specified.

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.

Blood sampling time will be related to the start of dosing. Linear and semi-logarithmic individual plasma concentration-time profiles (by randomized groups and by subject) and mean (±SD) and median profiles will be plotted for each randomized group. Plasma concentrations of bepirovirsen will be listed and summarised by randomized groups and nominal time. Summaries, including mean (±SD) and median profile plots, will also be produced by randomized group and injection site; and randomized group and baseline body weight category (CCI [redacted]); and randomized group, injection site and baseline body weight category (CCI [redacted]).

4.1.2. Baseline Definition

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline.

For ECG and/or Vital Signs analyses, if the last, non-missing pre-dose values is measured in triplicate, then the subject level baseline is defined as the mean of the triplicate baseline assessments.

Blood pressure and pulse will be measured in triplicate before dosing, single measurements after dosing. Single temperature and respiratory rate measurements will be measured at all time points. When measurement is repeated at the same time point then the mean will be used.

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

Baseline of serum creatinine is defined as the mean of all pre-dose values, from screening to Day 1 pre-dose assessment.

4.1.3. Plasma bepirovirsen concentration-time data Analysis

Plasma bepirovirsen concentration-time data will be analysed by the Clinical Pharmacology Modelling & Simulation department within GSK, using noncompartmental methods with Phoenix WinNonlin version 8.0 or higher. Statistical analysis will be performed by Biostatistics, GSK. Calculations will be based on the actual sampling times recorded during the study.

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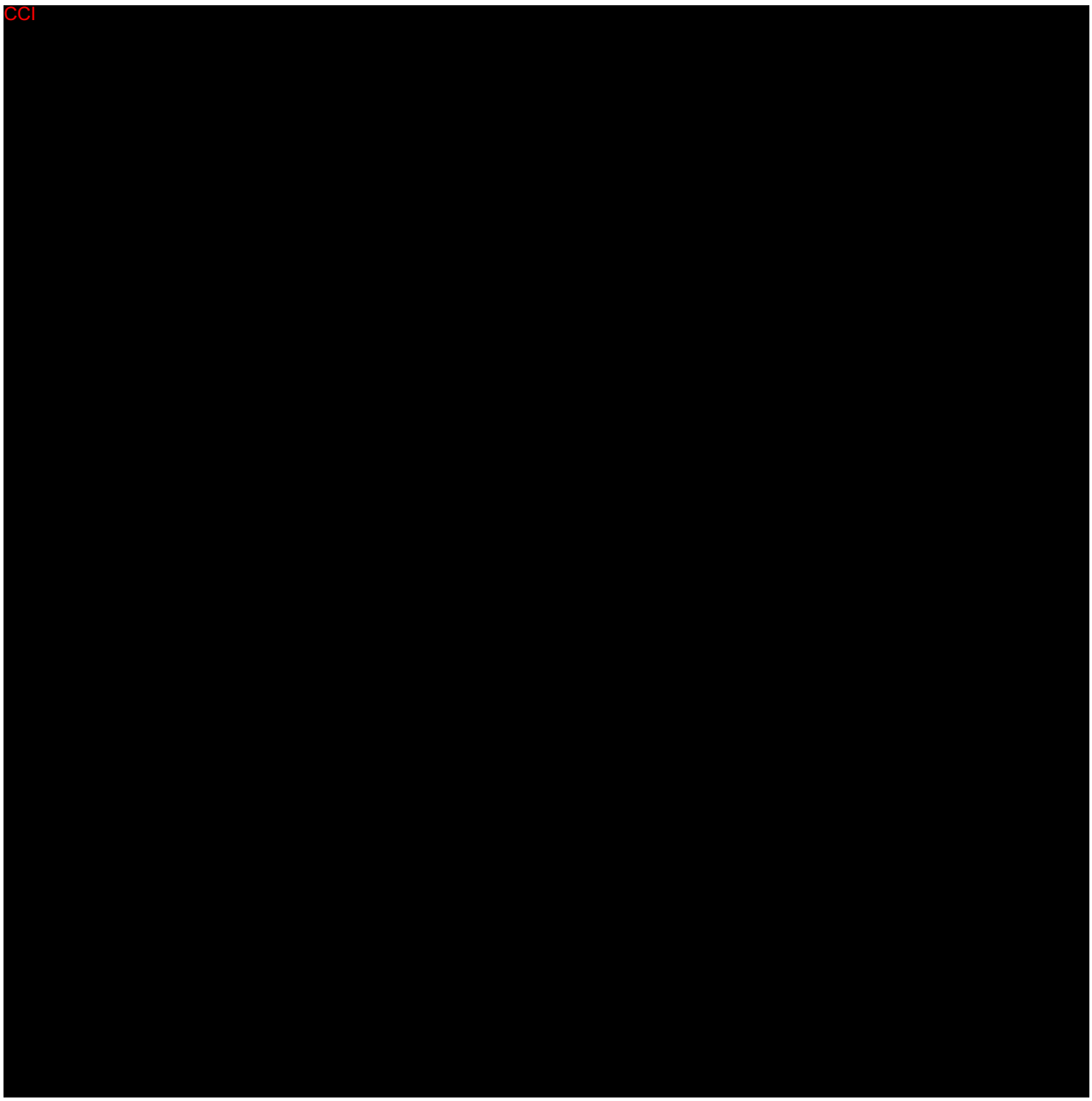

CCI

4.2.3. Supplemental estimands

A supplemental estimand to the primary objective assessing the impact of participants who were unable to take the complete dose. The estimand will be the same as the primary estimand except for the intercurrent event of incomplete dosing (participants who did not take CCI vials) which will now be considered using a treatment policy strategy.

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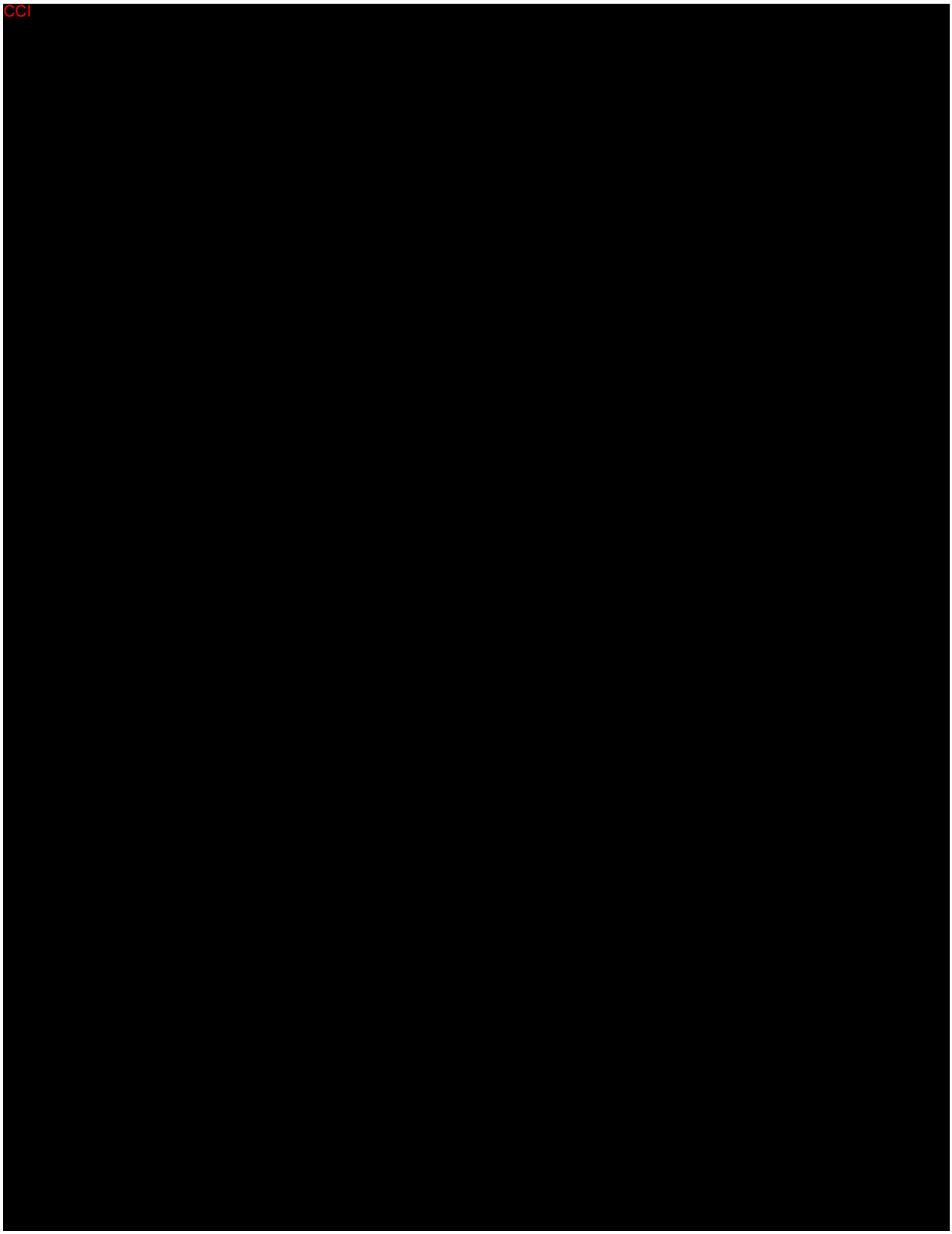

4.3.1.3. Sensitivity analyses

If large differences in exposure due to injection site in our primary endpoint analysis are observed, then a sensitivity analysis exploring injection site differences will be conducted

only for the secondary objectives using fixed effect models as specified in Section 4.3.1.2 and will be analysed and reported in a similar manner as described in Section 4.2.2. This analysis will only include those subjects from randomised group 2 where the injection site is thigh or abdomen.

4.3.1.4. Supplemental estimands

A supplemental estimand to the secondary objective assessing the impact of participants who were unable to take the complete dose will be considered as described in Section 4.2.3.

4.4. Exploratory Analyses

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4.4.3. Pharmacodynamic Effect of Bepirovirsen (Biomarker Analysis)

Additional details of the biomarker analysis will be provided in the biomarker analysis plan and the results will be documented in a separate report.

4.5. Safety Analyses

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

4.5.1. Adverse Events

An AE is considered treatment emergent (TEAE) if the AE onset date is on or after treatment start date. An AE is serious (SAE) if it results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect or in other situations described in Section 10.3 Appendix 3 of the protocol.

If AE start date is completely missing and the end date is on or after the treatment start date, the AE will be assumed to be treatment emergent. All AE summaries will be based on treatment emergent events unless otherwise specified.

Adverse events will be coded using the latest version of Medical Dictionary for Regulatory Affairs (MedDRA) coding dictionary, to give a Preferred Term (PT) and a System Organ Class (SOC). These PTs and SOCs will be used when summarising the data. The severity of AEs and SAEs will be determined by the investigator according to the Division of AIDS (DAIDS) grading system Version 2.1 [National Institute of Allergy and Infectious Diseases. Division of AIDS, 2017], unless specified otherwise in the protocol.

For AEs by maximum grade summary tables, if a participant reports an AE more than once within an SOC/PT, the AE with the most severe intensity will be included in summaries. Relationship to study treatment, as indicated by the investigator, is classified as “not related” or “related”. Adverse events with a missing relationship to study treatment will be regarded as “related” to study treatment.

The following table AE summaries will be presented for each randomized group:

1. AEs overview: summary of the number and percentage of participants with any adverse event, AEs related to study treatment, any SAEs, SAEs related to study treatment, fatal SAEs and fatal SAEs related to study treatment.
2. All AEs by SOC and PT.
3. All AEs by SOC and PT and maximum grade.
4. All treatment-related AEs by SOC and PT.
5. All treatment-related AEs by SOC and PT and maximum grade.
6. SAEs by SOC and PT.
7. Treatment-related SAEs by SOC and PT.
8. AEs leading to withdrawal from the study by SOC and PT.
9. AEs leading to withdrawal from the study by overall frequency.
10. Fatal AEs by SOC and PT.
11. Serious AEs by SOC and PT (number of participants and occurrences).
12. Serious Fatal and Non-Fatal Treatment-Related AEs by overall frequency.

Number of participants with AEs will be summarized if it is not specified otherwise.

In summary tables where AEs are presented by SOC, PT, and maximum grade, SOCs will be sorted in descending order of the total incidence then alphabetically, PTs will be sorted in descending order of the total incidence then alphabetically within the SOC.

Deaths will be summarized and listed including primary cause of death.

4.5.1.1. Adverse Events of Special Interest

The following AEs of special interest (AESI) will be reported to characterise the important potential risks (safety concerns) for bepirovirsen:

- ALT increase.
- Vascular inflammation and complement activation.
- Thrombocytopenia.
- Renal injury.
- Injection Site Reactions.

In addition, the following AEs which are identified as significant events but not as safety concerns will be reported:

- Immune-mediated events
- Neutropenia

An up-to-date list of standardized MedDRA Queries (SMQ)s, high level terms (HLTs) or individual PTs used to identify AESIs is periodically updated and stored in a central location. At the time of Database Lock (DBL), the latest version of the terms will be extracted and used to identify AESIs.

All AESIs and significant events will be summarized by SOC and PT, and summarized by SOC, PT, and maximum grade. Serious AESIs will be summarized by SOC and PT. All AESIs and significant events will be listed. Also, a listing of non-fatal SAEs will be produced.

Separate outputs will be created for each AESI and significant event category (ALT increase, vascular inflammation and complement activation, thrombocytopenia, renal injury, immune-mediated events, neutropenia, and injection site reactions) to explore the data in more detail if data permits.

Event Characteristics: The characteristics of all event occurrences during the post-baseline period will be summarized, which looks at event characteristics (serious, resulting in hospitalisation, drug-related, leading to withdrawal, maximum intensity, or maximum grade, fatal), number of events per participant, outcome, maximum grade or intensity and action taken. Event characteristics will be described by the proportion based on all subjects and the proportion based on subjects with the event for each of these items.

4.5.2. Additional Safety Assessments

4.5.2.1. Laboratory Data

Only central lab data will be used for summary analyses and figures; local lab data will be included in listings, as appropriate. The clinical laboratory tests are listed in Table 11 of protocol Section 10.2.

4.5.2.2. Laboratory Reporting

The haematology, clinical chemistry, urinalysis, and additional parameters to be tested are listed in the Appendix 2 of the Protocol.

Summary statistics for changes from baseline for each numeric parameter at each time point will be presented, separately for all clinical chemistry (along with liver function parameters) parameters, all haematology parameters, and all urinalysis parameters.

Also, summaries of worst-case grade increase from baseline grade will be provided for all the lab tests that are gradable by DAIDS grading system Version 2.1 [National Institute of Allergy and Infectious Diseases. Division of AIDS, July 2017]. These summaries will display the number and percentage of participants with a maximum post-baseline grade increasing from their baseline grade. For laboratory tests that are graded for both low and high values, summaries will be done separately and labelled by direction.

For lab tests that are not gradable by DAIDS Version 2.1, summaries of worst-case changes from baseline with respect to normal range will be generated. Decreases to low, changes to normal or no changes from baseline, and increases to high will be summarized for the worst-case post-baseline. If a subject has a decrease to low and an increase to high

during the same time interval, then the subject is counted in both the "Decrease to Low" categories and the "Increase to High" categories. Also, laboratory values outside of normal range will be listed.

Shift tables showing baseline toxicity versus maximum post-baseline toxicity for each grade (Grade1, Grade 2, etc.) for laboratory, chemistry and haematology parameters will be provided.

The worst-case urinalysis results post-baseline relative to baseline will be summarized.

Increase to Grade 3 or higher lab abnormalities for platelets, ALT, AST, , WBC, total bilirubin, serum creatinine, ACR will be summarized.

Scatter plots of maximum ALT vs baseline ALT as well as maximum total bilirubin vs maximum ALT will be presented. Also, plots showing mean actual and change from baseline values of the parameters over time will be presented. Listings of urinalysis data as well as lab data for subjects with values outside the normal range will also be created.

4.5.2.3. Monitoring Event Reporting

Liver monitoring and stopping event reporting will be summarized and listed. The Liver monitoring and stopping criteria are described in the protocol Section 7.1.1.

Haematological monitoring will be summarized and listed based on laboratory parameters (platelet count and anti-platelet antibodies). The haematological monitoring criteria are described in the protocol Section 7.1.2.

Data for potential Drug induced kidney injury (renal) monitoring events will be captured in the eCRF; they will be summarized. The kidney injury monitoring criteria are described in the protocol Section 7.1.3.

Data for potential drug induced vascular injury and complement monitoring will be captured in the eCRF; they will be summarized. The drug induced vascular injury and complement monitoring criteria are described in the protocol Section 7.1.4.

4.5.2.4. Vital Signs

Summary statistics for absolute values and change from baseline (by each time point and treatment group) in temperature, pulse rate, respiratory rate, systolic blood pressure (SBP), diastolic blood pressure (DBP) will be provided.

Also, by-treatment summaries of grade increase in temperature, SBP and DBP will be provided separately. These summaries will display the number and percentage of participants with any grade increase, increase to Grade 2, increase to Grade 3 and increase to Grade 4 (for temperature only), for worst case post-baseline only. The summaries will be produced for worst case post baseline only. The DAIDS grading system Version 2.1 [National Institute of Allergy and Infectious Diseases. Division of AIDS, 2017], will be used for grading: The grade definition for temperature is: Grade 1 (38.0°C – <38.6°C),

Grade 2 (38.6°C – <39.3°C), Grade 3 (39.3°C – <40.0°C), Grade 4 (≥40.0°C). The grade definition for SBP is Grade 1 (140-159), Grade 2 (160-179), Grade 3 (≥180). The grade definition for DBP is Grade 1 (90-99), Grade 2 (100-109), Grade 3 (≥110). DAIDs does not include a Grade 0, please refer to the OPS for instruction on how to present values that don't meet the criteria for Grade 1+. Participants with missing baseline values are assumed to have a normal baseline value.

4.5.2.5. ECG

When data is collected as triplicate, the average of triplicate ECG measures for each patient will be used.

ECG data (absolute values and change from Baseline) will be summarised by each timepoints and randomised groups only for the end of study analysis.

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[redacted]

4.7. Changes to Protocol Defined Analyses

There were no changes or deviations to the originally planned statistical analysis specified in the protocol. (Dated : [26th July 2023]).

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[redacted]

To assess the secondary objectives of estimating the relative bioavailability of Group 2 compared to Groups 3 and 4, approximately CCI subjects will be randomized into Groups 3 and 4 (approximately CCI per arm). This will provide the same number of subjects in the applicable sites of administration (thigh and abdomen) compared to Groups 1 and 2.

6. SUPPORTING DOCUMENTATION

6.1. Appendix 1 Study Population Analyses

Unless otherwise specified, the study population analyses will be based on the Safety Analysis Set. A summary of the number of participants in each of the participant level analysis set will be provided.

Study population analyses including analyses of participant disposition, demographic and baseline characteristics, protocol deviations, and prior and concomitant medications and medical history. Details of the planned displays are presented in the OPS document.

6.1.1. Participant Disposition

A summary of the number and percentage of patients who were screened including screen failures will be provided. Reasons for failure will be included.

A summary of the number and percentage of participants who completed the study, as well as those who prematurely withdrew from the study will be provided. Reasons for study withdrawal will be summarized.

Summaries of disposition, adverse events leading to withdrawal and reasons for withdrawal will be presented, as defined in the OPS.

Listings of reasons for study withdrawal, screen failure will be provided.

6.1.2. Demographic and Baseline Characteristics

Demographic characteristics including sex, age, ethnicity, race, height, and weight will be summarized with descriptive statistics.

Baseline characteristics including but not limited to BMI, hypertension, diabetes, serum creatinine, urine ACR, platelets, ANCA, complement C3, complement C4, C Reactive Protein will be summarized with descriptive statistics. Continuous characteristics will be presented using summary statistics (n, Mean, SD, Median, Min, Max) and may also be categorized and summarised using n (%).

Past medical conditions and current medical conditions as of screening will be summarized as “Summary of Past and Current Medical Conditions”.

Substance use, including smoking history, tobacco use, alcohol and drug history will be summarized.

6.1.3. Protocol Deviations

Important protocol deviations will be summarized and 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 are captured and categorised in the protocol deviations dataset.
- This dataset will be the basis for the summaries of important protocol deviations.

No per protocol analysis is planned for this study.

6.1.4. Prior and Concomitant Medications

Prior and concomitant medications will be coded using the newest versions of both the GSK Drug and the World Health Organization Drug Dictionary (WHODD). However, the summary will be based on GSK Drug dictionary only. The summary of concomitant medications will be provided by ingredient, i.e., multi-ingredient medications will be summarized for each individual ingredient rather than a combination of ingredients. The summary will be created using ingredient base names, i.e., ingredients with the same base name but different salt will appear under one base name in the summary. Anatomical Therapeutic Chemical (ATC) classifications will not appear in the summary, unless otherwise specified.

Concomitant medications will be summarized, where:

- A prior medication is defined as any medications that is started and ended prior to the date of single dose.
- Medications initiated after the single dose or initiated prior to the single dose and continued after the single dose will be counted as concomitant medications.

A medication that cannot be determined as prior or concomitant medication due to partially or completely missing start/stop date will be classified as the worst case, i.e., concomitant.

6.1.5. Study Intervention Compliance

Not Applicable.

6.2. Appendix 2 Data Derivations Rule

6.2.1. Study Period

Assessments and events will be classified according to the time of occurrence of relative dosing.

6.2.2. Study Day and Reference Dates

The safety reference date is the study intervention start date and will be used to calculate study day for safety measures.

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

Assessment windows are described in Table 3 of the protocol.

6.2.4. Multiple measurements at One Analysis Time Point

Mean of the measurements (e.g., ECG) will be calculated and used in any derivation of summary statistics but if listed, all data will be presented.

If there are two values within a time window the value closest to the target time 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 (including post-baseline unscheduled assessments) for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables.

6.2.5. Handling of Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays. • However, where necessary, display macros may impute dates as temporary variables for sorting data in listings only. In addition, partial dates may be imputed for 'slotting' data to study phases or for specific analysis purposes as outlined below.

<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
<tr><td></td><td>• 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.</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 intervention start date is missing (i.e. participant did not start study intervention), then set start date = 1st of month.

Else if study intervention start date is not missing:

• If month and year of start date = month and year of study intervention start date, then

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

– Else set start date = study intervention start date.

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

Else if study intervention start date is not missing:

• If year of start date = year of study intervention start date, then

– If stop date contains a full date and stop date is earlier than study intervention start date, then set start date = January 1.

– Else set start date = study intervention start 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
Concomitant Medications/Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention:	
	Missing start day	If study intervention start date is missing (i.e. participant did not start study intervention), then set start date = 1st of month. Else if study intervention start date is not missing: • If month and year of start date = month and year of study intervention start date, then – If stop date contains a full date and stop date is earlier than study intervention start date, then set start date= 1st of month. – Else set start date = study intervention start date. Else set start date = 1st of month.
	Missing start day and month	If study intervention start date is missing (i.e. participant did not start study intervention), then set start date = January 1. Else if study intervention start date is not missing: • If year of start date = year of study intervention start date, then – If stop date contains a full date and stop date is earlier than study intervention start date, then set start date = January 1.

Element	Reporting Detail	
		– Else set start date = study. intervention start date. Else set start date = January 1.
	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	A '31' will be used for the day and 'Dec' will be used for the month.
	Completely missing start/end date	No imputation
Age	• Age will be calculated based on the Pre-Screening Visit date (or Screening if pre-screening not performed).	

6.2.6. Abbreviations & Trademarks

Abbreviation	Description
ADA	Anti-drug antibody
AE	Adverse Event
AESI	Adverse Event of Special Interest
ATC	Anatomical Therapeutic Chemical
AUC	Area under concentration-time curve
AUC(0-inf)	Area under the concentration-time curve from time zero (pre-dose) extrapolated to infinite time
BMI	Body Mass Index
C	Complement
CI	Confidence Interval
C_{max}	Maximum Observed Concentration
CPMS	Clinical Pharmacology Modelling & Simulation
CSR	Clinical Study Report
CV	Coefficient of Variation
DBF	Database Freeze
ECG	Electrocardiogram
eCRF	Electronic Case Record Form
FTIH	First Time in Humans
GSK	GlaxoSmithKline
HLT	High Level Term
ICE	Intercurrent Event
MedDRA	Medical Dictionary for Regulatory Activities
n	Number of participants with available data
NCA	Non-compartmental Analysis

Abbreviation	Description
NONMEM	Non-linear Mixed-effects Modelling
OPS	Output and Programming Specification
PFS	Pre-filled Syringe
PK	Pharmacokinetic
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	Standard Deviation
SMQ	Standardized MedDRA Query
SOC	System Organ Class
SSD	Safety Syringe Device
WBC	While Blood Cell

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SAS
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7. REFERENCES

Hatcher RA, Trussell J, Nelson AL, Cates W Jr, Stewart F, Kowal D, eds. Contraceptive technology. 19th edition. New York: Ardent Media, 2007(a): 24. Table 3-2.