

# STATISTICAL ANALYSIS PLAN

## AN OPEN-LABEL, SINGLE-DOSE STUDY TO ASSESS THE CONCENTRATION OF ROZANOLIXIZUMAB IN THE BREAST MILK OF HEALTHY LACTATING WOMEN

### PROTOCOL UP0141

Short title: A study to assess rozanolixizumab in breast milk of healthy lactating women

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## LIST OF ABBREVIATIONS

ADE	adverse device effect
AE	adverse event
ASPS	all study participants set
BMI	body mass index
CI	confidence interval
CSR	clinical study report
CTR	clinical trial registry
DMC	data monitoring committee
DRM	data review meeting
ECG	electrocardiogram
eCRF	electronic case report form
EDV	early discontinuation visit
EMA	European Medicines Agency
FDA	US Food and Drug Administration
HLT	high level term
ICH	International Council for Harmonisation
IMP	investigational medicinal product
IPD	important protocol deviation
LLOQ	lower limit of quantification
MedDRA	Medical Dictionary for Regulatory Activities
PD	protocol deviation
PK	pharmacokinetic
PKS	pharmacokinetic set
PT	preferred term
SADE	Serious adverse device effect
SAP	statistical analysis plan
sc	subcutaneous
SOC	system organ class
SS	safety set
TEAE	treatment-emergent adverse event

## STATISTICAL ANALYSIS PLAN AMENDMENT SUMMARY OF CHANGES TABLE

The Statistical Analysis Plan (SAP) for study UP0141 is based on the protocol dated 11 September 2024.

### Document history

Document	Date	Change	Rationale
Original SAP	28FEB2025	Not Applicable	Original document

# 1 INTRODUCTION

The purpose of this SAP is to provide all information that is necessary to perform the required statistical analysis of UP0141. It also defines the summary tables, figures and listings (TFLs) to be included in the final clinical study report (CSR).

If a future protocol amendment necessitates a substantial change to the statistical analysis of the study data, this SAP will be amended accordingly. In addition, if the methodology for the analysis of key endpoints must be modified or updated prior to database lock, a SAP amendment will be required. If, after database lock, additional analyses are required to supplement the planned analyses described in this SAP, these changes will be described in the CSR together with the associated rationale. Other minor changes to non-key analyses will also be documented in the CSR.

The content of this SAP is compatible with the International Council for Harmonisation (ICH)/Food and Drug Administration (FDA) E9 Guidance document (CPMP/ICH/363/96, 1998).

## 1.1 Objectives and endpoints

**Table 1-1: Objectives and endpoints**

Objectives	Endpoints
<b>Primary</b>	
<ul style="list-style-type: none"> <li>To assess the concentration of rozanolixizumab in mature breast milk of healthy study participants following administration of a single dose of rozanolixizumab</li> </ul>	<p>The primary PK endpoint is concentration of rozanolixizumab in breast milk over a 7day Sampling Period.</p> <p>The secondary PK endpoints are:</p> <ul style="list-style-type: none"> <li>Estimated daily infant dosage</li> <li>Relative infant dose of rozanolixizumab from breast milk</li> </ul>
<b>Secondary</b>	
<ul style="list-style-type: none"> <li>To assess the safety of a single dose of rozanolixizumab administered to healthy study participants</li> </ul>	<p>The secondary safety endpoint is occurrence of TEAEs from Day 1 through the SFU Visit.</p>
<b>Exploratory/Other</b>	
<ul style="list-style-type: none"> <li>To determine PK parameters of rozanolixizumab in mature breast milk and plasma of healthy study participants following administration of a single dose of rozanolixizumab</li> </ul>	<p>The exploratory/other PK endpoints are:</p> <ul style="list-style-type: none"> <li><math>C_{max}</math>, <math>t_{max}</math>, <math>AUC_{(0-7d)}</math> in breast milk and plasma</li> <li><math>Ae_{7d}</math> and Fe in breast milk</li> <li>Milk:plasma <math>AUC_{(0-7d)}</math> ratio</li> </ul>

$Ae_{7d}$ =cumulative total amount of drug excreted in milk to Day 7;  $AUC_{(0-7d)}$ =area under the concentration-time curve from 0 to 7 days; d=day;  $C_{max}$ =maximum plasma or milk concentration; Fe=fraction of dose excreted in milk; PK=pharmacokinetic(s); SFU=Safety Follow Up; TEAE=treatment emergent adverse event;  $t_{max}$ =time to maximum plasma or milk concentration

## 1.2 Study design

This is a post marketing, open-label, Phase 1 (Clinical Pharmacology) study to assess the concentration of rozanolixizumab in mature breast milk of healthy lactating women following administration of a single dose of rozanolixizumab.

The study will enroll healthy lactating women (herein referred to as study participants) who on Day 1 of the study (rozanolixizumab dosing day) will be at least 6 weeks postpartum and who have voluntarily decided, prior to having knowledge of the study, to wean their infant(s). On Day 1, study participants will receive a single dose of rozanolixizumab, administered subcutaneously. The dosage will be based on the participants' body weight on Day 1 (420 mg for participants <50 kg, 560 mg for participants  $\geq 50$  kg to <100 kg, or 840 mg for participants  $\geq 100$  kg).

Additionally, to be eligible to participate in the study, participants must agree to collect all expressed breast milk over the 7-day Sampling Period and to not resume breast milk feeding (by any means) or donate expressed breast milk between the end of the breast milk Sampling Period and the SFU telephone call 8 weeks after dosing (i.e., on Day 57). Participants may decide to resume breast milk feeding 8 weeks after administration of rozanolixizumab, with the agreement that any breast milk collected (to maintain milk supply) during that 8-week period will be discarded. A lactation consultant will be available from the Screening Period up until 30 days after the SFU telephone call to support the cessation and potential resumption of breast milk feeding following the SFU. Details of when samples of breast milk and plasma are collected are outlined in Section 1.3 of the protocol.

Up to 20 healthy study participants are planned to be screened to ensure that a minimum of 12 study participants and a maximum of 15 study participants provide data to assess whether there is transfer of rozanolixizumab into breast milk. The study is planned to be conducted in the United States.

For each study participant, the total duration of participation in this study is up to 12 weeks, including a Screening Period of up to 4 weeks, a Sampling Period of 7 days, including an In Clinic Period from Day 1 (or Day 1) to Day 3, and a SFU telephone call 8 weeks after dosing (i.e., on Day 57) (Section 1.3 of the protocol). During the Sampling Period, on Day 1, study participants will receive a single dose of rozanolixizumab based on their body weight (Table 4-1 in the protocol).

## 2 STATISTICAL HYPOTHESES

Not applicable.

### 2.1 Multiplicity adjustment

Not applicable.

## 3 ANALYSIS SETS

The following are the defined analysis sets:

- All Study Participants Set (ASPS): All study participants who sign the ICF.
- Safety Set (SS): All study participants who receive a full or partial dose of the IMP.

- PK Set (PKS) (for breast milk and plasma): All study participants in the SS who receive a full dose of the IMP and provide at least 1 valid measurement of rozanolixizumab concentration in plasma or breast milk. A valid measurement of rozanolixizumab concentration in breast milk or plasma may include BLQ values.

## **4 STATISTICAL ANALYSIS**

### **4.1 General considerations**

Tables, figures and listings (TFLs), including statistical evaluation, will be produced by UCB. Standard reporting will use SAS version 9.4 or higher (SAS Institute, Cary, North Carolina, USA). Analysis data will adhere to Clinical Data Interchange Standards Consortium (CDISC) guidance documents for Analysis Data Model (ADaM). The PK noncompartmental analysis (NCA) will be performed using Phoenix WinNonlin® v8.0 or higher (Certara L.P., Princeton, NJ, USA) for pharmacokinetics parameters calculation.

Descriptive statistics will be displayed to provide an overview of the study results, and study participant data listings are generated for relevant (as according to ICH E3 (CPMP/ICH/137/95, 1996)) reported and/or calculated data.

Tables and figures will be presented by visit and timepoint where applicable.

For continuous endpoints, descriptive statistics will include number of study participants with available measurements (n), mean, standard deviation (SD), median, minimum and maximum. Geometric mean (geoMean), geometric standard deviation (geoSD), geometric coefficient of variation (geoCV) and 95% CI for the geoMean will also be presented in the summaries of PK concentration data and PK parameters.

Decimal places for descriptive statistics (except for PK) will apply the following rules:

- “n” will be an integer.
- Mean, SD, and median will use 1 additional decimal place compared to the original data.
- Coefficient of variation (CV[%]) will be presented with 1 decimal place.
- Minimum and maximum will have the same number of decimal places as the original value.

For rules of reporting PK concentration data and PK parameters, refer to Section 6.10.

For categorical endpoints, the number and percentage of study participants in each category will be presented. The denominator for percentages will be based on the number of study participants in the non-missing categories. Unless otherwise noted, all percentages will be displayed to 1 decimal place. No percentage will be displayed for zero counts, and no decimal will be presented when the percentage is 100%.

If no participants have data at a given timepoint, then only n=0 will be presented. If n<3, then only the n, minimum, and maximum will be presented. If n=3, then only n, minimum, median, and maximum will be presented. The other descriptive statistics will be left blank.

#### **4.1.1 Analysis time points**

##### **4.1.1.1 Study periods**

The study periods are as follows:

- Screening Period (Visit 1: Day -28 to -1)
- Sampling Period (Visits 2 to 8: Days 1 to 7)
- SFU Period (Days 8 to 57)

A study participant is considered to have completed the study if she has completed all periods of the study including the SFU period and did not discontinue the study early.

Visit 9 is a SFU telephone call which will occur on Day 57 ( $\pm 5$  days).

#### 4.1.1.2 Visit variables

The visit variables will be reported in the TFLs as per [Table 4-1](#).

**Table 4-1: Visit variables**

Visit name in the protocol	Visit variable to be displayed in TFLs
V1 (Week -4 to -1, Day -28 to -1)	Screening
V2 (Week 1, Day 1)	Day 1
V3 (Week 1, Day 2)	Day 2
V4 (Week 1, Day 3)	Day 3
V5 (Week 1, Day 4)	Day 4
V6 (Week 1, Day 5)	Day 5
V7 (Week 1, Day 6)	Day 6
V8 (Week 1, Day 7)	Day 7
EW (Week 1, Day 7)	Early Withdrawal
SFU (Week 9, Day 57)	Day 57 (SFU)

EW=early withdrawal, SFU=safety follow-up, V=visit.

Note: Early Withdrawal should only be used for participants who terminate the study early.

#### 4.1.1.3 Relative day for listings

Relative day for an event or measurement occurring before the date of the first dose will be calculated as follows:

$$\text{Relative Day} = \text{Event/Measurement Date} - \text{Date of First Dose}$$

Relative day for an event or measurement occurring on the date of the first dose is 1.

Relative day for an event or measurement occurring on the date of the first dose will be calculated as follows:

$$\text{Relative Day} = (\text{Event/Measurement Date} - \text{Date of First Dose}) + 1$$

Relative day for an event or measurement occurring after the date of the first dose to the date of the last visit will be calculated as follows:

$$\text{Relative Day} = +(\text{Event/Measurement Date} - \text{Date of First Dose})$$

There is no relative day 0. Relative day will not be calculated for partial dates, instead relative day will be presented as '--' in the relevant participant data listing.

#### 4.1.1.4 Handling of repeated and unscheduled measurements

All repeated and unscheduled measurements will be presented in the listings, where applicable. The following general rules will apply to all repeated and unscheduled measurements, unless otherwise specified:

- For repeated or unscheduled measurements obtained prior to the first dose of IMP the latest non-missing value (scheduled or unscheduled) will be used in the calculation of descriptive statistics (i.e. Baseline);
- For repeated or unscheduled measurements obtained at any time point after the first dose of IMP, the scheduled values (if non-missing) will always be used in the calculation of changes from Baseline and for the descriptive statistics (i.e., in summaries by time point). If repeated scheduled values are obtained at any time point, the latest non-missing values will be used.

#### 4.1.2 Definition of baseline values

Baseline for vital signs, hematology, clinical chemistry, or urinalysis measurements is defined as the last available measurement (scheduled or unscheduled) prior to dosing.

#### 4.1.3 Date Imputation

Partial dates/times may be imputed for the following purposes:

- Classification of adverse events (AEs) as treatment emergent
- Calculation of AE durations
- Classification of medications as past, prior, or concomitant

Imputed dates will not be shown in the listings; all dates will be displayed as reported in the database. Any partial dates should be queried and resolved prior to database lock (DBL).

The following rules will be applied for partially or completely missing start dates and times:

- If the **day** is missing, and the year and month are:
  - the same as the month-year of the first dose of IMP then assign the day of first dose of IMP. If the imputed start date is after the specified end date, then assign the day of screening date. If this results in the imputed start date is after the specified end date, then assign the first of the month;
  - not the same as the month-year of the first dose of IMP then assign the first of the month.
- If **month and day are missing**, and year is:
  - the same as the year of the first dose of IMP then assign the month-day of first dose of IMP. If the imputed start date is after the specified end date, then assign the month-day of screening date. If this results in the imputed start date is after the specified end date, then assign January 01;

- not the same as the year of the first dose of IMP then assign January 01.
- If **year, month and day are all missing** then assign the date of first dose of IMP. If an imputed start date is after the specified end date, then assign January 01 of the year of the end date, or the date of screening if this is later (if the latter imputation results in an end date that is earlier than the start date, then use January 01).
- If the **time** is missing, then assign time of first dose of IMP, if not missing. Otherwise, impute start time as 00:00h.

The following rules will be applied for partially or completely missing end dates and times:

- If the **day** is missing, then use the last day of the month. If an imputed stop date is after last contact date and last contact date is before the data cut-off date, then assign last contact date as the stop date. If an imputed stop date is after last contact date and last contact date is after the data cutoff date, then assign data cutoff date as the stop date.
- If **month and day** are missing, then use December 31 of the known year. If an imputed stop date is after last contact date and last contact date is before the data cutoff date, then assign last contact date as the stop date. If an imputed stop date is after last contact date and last contact date is after the data cutoff date, then assign data cut-off date as the stop date.
- If **year, month and day** are all missing, then use discharge date or data cut-off date.

Discharge date refers to the date of the end of study visit for completed participants or the date of discontinuation for participants that were withdrawn. For any AEs with known start date after the date of discontinuation, the date of last contact will be used as the discharge date. For participants still ongoing in the study at the time of the data cut-off, and for whom no discharge date is available, the date of the data cut-off will be used instead of the discharge date.

- If the **time** is missing, then set to 23:59h.

Any medication with a start date on the first dosing date will be assumed to be concomitant.

Any level of imputed AE dates and times will be used for the calculation of duration of AEs as described in Table 4-2. Duration will be displayed in listings as days, hours and minutes.

**Table 4–2: Calculation rules for duration of adverse events**

Data availability	Calculation rules
Complete start and end date/times	Duration = end datetime – start datetime
Start date or time imputed	Duration <= end datetime – start datetime
End date or time imputed	For ongoing AEs: <ul style="list-style-type: none"><li>● Duration &gt;= end datetime – start datetime</li></ul> For resolved AEs: <ul style="list-style-type: none"><li>● Duration &lt;= end datetime – start datetime</li></ul>

**Table 4–2: Calculation rules for duration of adverse events**

Data availability	Calculation rules
Start and end date or time imputed	<p>For ongoing AEs:</p> <ul style="list-style-type: none"> <li>Duration <math>\geq</math> end datetime – start datetime</li> </ul> <p>For resolved AEs:</p> <p>Duration <math>\leq</math> end datetime – start datetime</p>

#### 4.1.4 Multicenter studies

Up to two study centers/sites in the US will be used in this study. Study participants will be assigned a unique study participant number which will include a center/site identification number, but no analysis by study center/site will be performed.

#### 4.1.5 Center pooling strategy

If more than one center/site in the US is used in this study, all the data will be pooled together in summaries.

### 4.2 Primary endpoints analysis

#### 4.2.1 Pharmacokinetics

##### 4.2.1.1 Definition of endpoints

The primary PK endpoint is the concentration of rozanolixizumab in breast milk over the 7 day Sampling Period.

The secondary PK endpoints that fall under the primary objective of the study are the estimated daily infant dosage and the relative infant dose of rozanolixizumab from breast milk.

#### Estimated daily infant dosage from breastmilk

The estimated daily infant dosage of rozanolixizumab from breast milk will be calculated based on the concentration of rozanolixizumab in mature human breast milk for the PKs.

The amount of rozanolixizumab that the infant may consume following single rozanolixizumab dosing to the mother will be calculated as follows:

$$1. \text{ Estimated daily infant dosage (mg/kg/day)} = \text{M/P ratio} \times C_{\text{av,plasma}} \times 150\text{mL/kg/day}$$

Where M/P ratio is the milk:plasma ratio based on  $\text{AUC}_{(0-7\text{d})}$  and  $C_{\text{av,plasma}}$  is the average maternal plasma concentration calculated as  $\text{AUC}_{(0-7\text{d}),\text{plasma}}/7 \text{ days}$ .

This is based on the standardized mean milk consumption for a fully breastfed 2-month old infant of 150mL/kg/day.

$$2. \text{ Daily infant dosage (mg/day)} = \sum (\text{total drug concentration in each breast milk collection} \times \text{the expressed milk volume (ml) in each collection}) \text{ for each 24hour period of the 7 days postdose.}$$

#### Relative infant dose from breast milk

The relative infant dose of rozanolixizumab from breast milk will be calculated as follows:

$$\text{Estimated daily infant dosage (mg/kg/day)} / \text{maternal rozanolixizumab dosage (mg/kg/day)} \times 100$$

Where

maternal rozanolixizumab dosage (mg/kg/day)=Actual dose administered/(Day 1 weight\*7)

Plasma PK endpoints will be computed using actual blood sampling time points.

The following exploratory PK parameters will be derived for rozanolixizumab in breast milk:

- $C_{max}$ ,  $t_{max}$ ,  $AUC_{(0-7d)}$
- $Ae_{7d}$  (mg)=cumulative total amount excreted in milk to Day 7
- $Fe=Ae_{7d}/\text{administered dose (mg)} \times 100\%$
- Milk:plasma  $AUC_{(0-7d)}$  ratio

The following exploratory PK parameters will be derived for rozanolixizumab in plasma:

- $C_{max}$ ,  $t_{max}$ ,  $AUC_{(0-7d)}$

### Supporting calculations

The time postpartum on Day 1 will be calculated as:

Time postpartum on Day 1 (weeks) = (Date of dosing - Date of delivery of infant(s))[days]/7

The single maternal dosage levels of rozanolixizumab will be based on body weight on Day 1 predose as follows:

420mg for study participants <50kg,

560mg for participants  $\geq 50\text{kg}$  to <100kg, or

840mg for participants  $\geq 100\text{kg}$

Actual dose administered will be calculated as:

Actual dose administered = Dosage level x Percent of planned dose administered

Where

Percent of planned dose administered = total volume delivered / total volume planned

The total volume planned is recorded in the eCRF.

#### 4.2.1.2 Main analytical approach

All PK analyses will be presented on the PKS.

The concentration of rozanolixizumab in breast milk and plasma will be listed and summarized using descriptive statistics by nominal (scheduled) sampling time points for the PKS. Any plasma concentrations with an actual sampling time deviation of greater than 10% from nominal sampling time will be flagged and excluded from the summary statistics, but will be included in the PK parameter calculations.

Individual study participant concentration-time profiles for rozanolixizumab in breast milk and plasma will be displayed together graphically on the linear and semi-logarithmic scale. Spaghetti plots of the individual concentration-time profiles will be displayed graphically (linear and semi-logarithmic scales) separately for milk and plasma. Geometric mean profiles of rozanolixizumab

concentrations in breast milk and plasma over nominal (scheduled) time will be displayed together graphically on the linear and semi-logarithmic scale. The 95% CIs for the geoMean will be displayed on the linear scale plot only and the LLOQ will be included on all semi-logarithmic scale plots. The midpoint of each milk sampling interval will be used in the plots for both the actual and nominal sampling times for the breast milk concentrations.

The estimated daily infant dosage and relative infant dose will be listed and summarized using descriptive statistics. The amount of rozanolixizumab excreted in each collection interval, and the daily infant dosage (or total amount of rozanolixizumab excreted for each 24-hour milk collection period) will be listed and summarized over the 7 days postdose,

The exploratory PK parameters will be listed and summarized separately for milk and plasma using descriptive statistics.

### **4.3 Secondary endpoints analysis**

#### **4.3.1 Treatment-emergent adverse events**

##### **4.3.1.1 Definition of endpoint**

All adverse events (AEs) will be coded using MedDRA<sup>®</sup> version 27.1 and characterized as pretreatment and treatment emergent according to the intake of treatment. Adverse events with a start date prior to the first and only dose of treatment will be defined as pretreatment AEs. A TEAE is defined as any AE with a start date/time on or after the dosing of study medication until 8 weeks (56 days) inclusive after dosing of study medication.

##### **4.3.1.2 Main analytical approach**

The number and percentage of participants who experience TEAEs will be summarized by MedDRA SOC, HLT, and PT. Summaries of TEAEs include, but are not limited to the following:

- Incidence of overall TEAEs (overview including number and percentage of participants with any TEAEs, serious TEAEs, discontinuations due to TEAEs, drug-related TEAEs, severe TEAEs, TEAEs leading to death, all deaths, TEAEs of Special Interest (Hy's Law), TEAEs of Special Monitoring, TEAEs of focus, ADEs, severe ADEs, and SAEs; event counts will also be included)
- Incidence of all TEAEs
- Incidence of Serious TEAEs
- Incidence of TEAEs by maximum intensity
- Incidence of TEAEs by maximum relationship
- Incidence of non-serious TEAEs above reporting threshold of 5% of study participants
- Incidence of all TEAEs by Preferred Term
- Discontinuation due to AEs
- Incidence of Serious TEAEs by Relationship
- Incidence of Fatal TEAEs by Relationship

Summary tables will contain counts of study participants, percentages of study participants in parentheses and the number of events where applicable. A participant who has multiple events in the same SOC, HLT, and PT during a given treatment will be counted only once in the participant counts for that treatment, but all events will be included.

Rozanolixizumab treatment-emergent adverse events of focus (TEAEOF) will also be analysed for the SS. TEAEOF are defined in Section 6.8. The number of and percentage of study participants who experience each category of the TEAEOF will be summarized. The following summaries will be presented by SOC, HLT and PT:

- Incidence of TEAEOF
- Incidence of Serious TEAEOF

In summaries including relationship, the following relationships will be summarized: 'Not related' and 'Related'. Participants who experience the same event multiple times will be included in the most related category for tabulations by maximum relationship. Events with missing relationship will be considered as 'Related' but recorded as missing in the listings.

In summaries including intensity, the following intensity categories will be summarized: 'Any', 'Mild', 'Moderate', and 'Severe'. Participants who experience the same event multiple times will be included in the most severe category for tabulations by maximum intensity. Events with missing intensity will be considered as 'Severe' events for summary purposes but recorded as missing in the listings.

Adverse event summaries will be ordered alphabetically by SOC and HLT within SOC, and by decreasing incidence of PT within HLT in the group column.

All AEs will be presented for the ASPS in the listings by study participant and will include the onset date/time and outcome date/time of the event, the event duration (derived), time to onset (derived), pattern of event, intensity, relationship to study drug, breast milk pump or drug delivery device, action taken, outcome and AEs that led to discontinuation.

Device deficiencies for the breast milk pump and drug delivery device will be listed for the ASPS.

### **4.3.2 Pharmacokinetics**

#### **4.3.2.1 Definition of endpoint**

The secondary PK endpoints are defined in Section 4.2.1.1 .

#### **4.3.2.2 Main analytical approach**

The main analytical approach is documented in Section 4.2.1.2 .

### **4.4 Exploratory endpoints analysis**

#### **4.4.1 Other pharmacokinetics**

The exploratory PK endpoints are described in Section 4.2.1.

### **4.5 Other Safety analysis**

In general, safety analyses will be presented on the SS unless stated otherwise.

#### 4.5.1 Vital signs

Vital signs will be measured in a semi-supine position after 5 minutes rest. The following vital signs measurements will be assessed:

- Systolic and diastolic blood pressure (BP)
- Pulse rate
- Body temperature
- Respiratory rate

The criteria for assessing if a vital sign value is abnormal is given in [Table 4–3](#).

Vital signs measurements will be summarized by visit and time point (where applicable) including observed values and changes from Baseline.

**Table 4–3: Criteria for abnormal vital signs**

Parameter	Unit	Abnormality Criteria
Systolic blood pressure	mmHg	$\leq 90$ and a decrease from Baseline of $\geq 20$ $\geq 180$ and an increase from Baseline of $\geq 20$
Diastolic blood pressure	mmHg	$\leq 50$ and a decrease from Baseline of $\geq 15$ $\geq 105$ and an increase from Baseline of $\geq 15$
Pulse rate	Beats/minute	$\leq 50$ and a decrease from Baseline of $\geq 15$ $\geq 120$ and an increase from Baseline of $\geq 15$
Body temperature	°F	$> 101$ (38.3 °C)

#### 4.5.2 Clinical laboratory evaluations

Treatment-emergent marked abnormalities (TEMA) in laboratory parameters may be analyzed. Thresholds for defining marked abnormalities for relevant laboratory parameters are available in [Appendix 6.11.1](#). MA values are considered treatment-emergent if the MA was not present before the date of first administration of the study drug and occurred on or after the date of the first administration of the study drug and before the end of the study.

Measurements below the lower limit of quantification (BLQ) will be imputed with half of the lower limit of quantification (LLOQ), and measurements above the upper limit of quantification (ALQ) will be imputed to the upper quantification limit for purposes of quantitative summaries.

Listings of clinical chemistry and hematology laboratory results will be produced for participants who had a value outside the normal ranges, including any values which are clinically significant as assessed by the investigator. These listings will include all data for each parameter for which a participant has at least one abnormal value during the study. Laboratory variables will be grouped according to the laboratory function panel (e.g., lipids, endocrine) and will be categorized as normal, high or low, if applicable, based on the reference range supplied by the analytical laboratory.

Clinical chemistry and hematology parameters will be summarized by visit for both absolute values and changes from Baseline.

Liver function laboratory results will be listed for study participants with elevated liver function results.

Urinalysis laboratory results will be listed but not summarized.

### 4.5.3 Electrocardiogram

A single 12-lead ECG will be obtained at Screening only. The following ECG parameters will be reported:

- Heart rate
- PR interval
- QT interval
- QRS interval
- QTc intervals (QT corrected for heart rate using Fridericia's formula [QTcF] and Bazett's formula [QTcB])

The criteria for assessing if an ECG parameter is abnormal is given in [Table 4-4](#). ECG parameters and any findings will be listed for the SS.

**Table 4-4: Criteria for abnormal ECG parameters**

Parameter	Unit	Abnormality Criteria
Heart rate	Beats/minute	< 50 or > 120
QT interval	ms	≥ 500
QTcF interval	ms	≥ 500
PR interval	ms	> 200
QRS interval	ms	> 100

### 4.5.4 Physical examination

Study participants with abnormalities in the physical examination will be listed including details of the abnormality and clinical significance.

### 4.5.5 Neurological evaluation

A full neurological examination will be performed for any participant who experiences severe and/or serious headache and for study participants who experience aseptic meningitis.

Study participants with abnormalities in the neurological examination will be listed including details of the abnormality and clinical significance.

### 4.5.6 Extent of exposure

Administration of treatment will be listed and will include the date of infusion, start and stop time of infusion, duration of infusion, whether the infusion was temporarily stopped or discontinued, and total volume of treatment given.

The duration of the sc infusion will be calculated as follows and will be presented in minutes:

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Duration (minutes) = Stop time – Start time.

#### **4.5.7 Additional safety assessments**

Additional laboratory test results including alcohol urine test, urine drug screen, and serum and urine pregnancy tests will be listed for the SS.

Prior and concomitant medical procedures will be listed for the SS.

#### **4.6 Other analyses**

Not applicable.

##### **4.6.1 Subgroup analyses**

Not applicable.

#### **4.7 Interim analyses**

Not applicable.

#### **4.8 Changes to protocol-planned analyses**

The definitions of past, prior, and concomitant medications have changed from the protocol and are documented in Section 6.6.

#### **4.9 Data Monitoring Committee or other review board**

Not applicable.

### **5 SAMPLE SIZE DETERMINATION**

No formal sample size calculations have been performed as there are no statistical hypotheses being tested. It is expected that up to 20 healthy study participants will need to be screened to ensure that a minimum of 12 participants and a maximum of 15 participants provide data to assess whether there is transfer of rozanolixizumab into breast milk after a single dose and to calculate the estimated daily infant dosage and relative infant dose from breast milk. This number was selected based on feasibility and considered to be sufficient to meet the primary objective.

## **6 APPENDIX: SUPPORTING DOCUMENTATION**

### **6.1 Appendix 1: Coding dictionaries**

The medical history and adverse events (AEs) will be coded using MedDRA 27.1. Medications will be coded using the World Health Organization Drug Dictionary (WHO-DD) B3 MAR/2024. Medical procedures and device deficiencies will not be coded.

### **6.2 Appendix 2: Disposition of study participants**

Study participant disposition will be listed for the ASPS and will include the following information: study participant status (screen failure, completed or discontinued), date of informed consent, date of IMP administration, and date of premature study and/or study drug termination (if applicable).

Study participant disposition will be summarized for the ASPS. The disposition table will include the reasons for screen failure, the number of study participants starting the Sampling

Period, the number of study participants completing the study, and reasons for discontinuation of study.

The study participants included in each of the analysis sets will be listed and summarized for the ASPS.

### 6.3 Appendix 3: Baseline characteristics and demographics

A listing of demographics by study participant will be presented for the ASPS. This will include the year of birth, age (in years), race, ethnicity, height (cm), weight at Screening and Day 1 predose (kg), body mass index (BMI, in kg/m<sup>2</sup> to 1 decimal place) at Screening and Day 1 predose, and time postpartum on Day 1.

All demographic characteristics taken at Screening (except for year of birth) will be summarized for the ASPS. The summary of age will include descriptive statistics and categorical summaries, the latter based on requirements for European Union Drug Regulating Authorities Clinical Trials (EudraCT) reporting.

For the EudraCT reporting, the categories will include:

- 18 to <65 years
- 65 to <85 years
- ≥85 years

BMI in kg/m<sup>2</sup> is calculated based on the height (in m) at Screening and the weight at Screening or Day 1 predose (in kg) using the following formula (if height is in cm, then height will be converted to meters by dividing by 100):

$$BMI (kg/m^2) = weight (kg) / [height (m)]^2$$

The BMI will be derived and automatically reported to 1 decimal place on the eCRF.

### 6.4 Appendix 4: Protocol deviations

All protocol deviations will be reviewed at the Data Cleaning Meetings (DCM) and decisions made on whether they should be considered important or not.

Important protocol deviations (IPDs) are deviations from the protocol which could potentially have a meaningful impact on study conduct or on either the primary or secondary outcome(s) for an individual study participant. The criteria for identifying such protocol deviations will be defined within the PD specifications document.

All protocol deviations will be categorized as follows:

- Inclusion/exclusion criteria deviations
- Incorrect treatment or dose administered
- Procedural non-compliance
- Prohibited concomitant medication use
- Withdrawal criteria deviation
- Other

Should a participant be mistakenly dosed despite failing the inclusion/exclusion criteria, then their safety data would need to be reported as part of the safety analysis. Participants may be excluded from other analysis sets, but this will be determined on a case-by-case basis. If the deviation is deemed to have the potential to bias the analyses for the duration of the study, then the whole participant may be removed in a sensitivity analysis on the key endpoints. The removal of the participant and the rationale will be clearly documented within the relevant TFLs.

Important protocol deviations will be identified and classified by the deviation types. A listing of all IPDs will be presented for all participants in the safety set and will include the deviation type and description.

The IPDs will be tabulated using the SS and will present the deviation type and description.

## 6.5 Appendix 5: Medical history

Medical history and ongoing medical conditions will be summarized for the SS by system organ class (SOC) and preferred term (PT). The summary will include the number and percentage of study participants and will be sorted alphabetically by SOC and by descending incidence of PT within each SOC.

## 6.6 Appendix 6: Past/prior/concomitant medications

For the purposes of this study:

- **Past medications** include those that started and stopped prior to administration of the study drug.
- **Prior medications** include those that started prior to administration of the study drug and either stopped prior to administration of the study drug or continued after administration of the study drug.
- **Baseline medications** include those that started prior to administration of the study drug and continued after administration of the study drug.
- **Newly concomitant medications** include those that started any time between administration of the study drug until the SFU Visit.
- **Concomitant medications** include both baseline and newly concomitant medications, being those that have been taken at least once between the administration of the study drug and the SFU Visit.

Past, baseline (includes prior/concomitant) and newly concomitant medications will be summarized based on the SS. These classifications of medications will be summarized in separate tables. The tables will be sorted alphabetically by Level 1 term, alphabetical Level 3 term within Level 1 and decreasing frequency of PT.

Past, baseline (includes prior/concomitant), and newly concomitant medications will be listed for the SS.

## 6.7 Appendix 7: AEs of special interest/special monitoring

Adverse events of special interest and AEs of special monitoring will be listed for the ASPs. If there are any events, AESIs and AESMs will be summarized for the SS.

### 6.7.1 AEs of Special Interest

Potential Hy's Law is defined as  $\geq 3$ x upper limit of normal (ULN) alanine aminotransferase (ALT) or aspartate aminotransferase (AST) with coexisting  $\geq 2$ xULN total bilirubin in the absence of  $\geq 2$ xULN alkaline phosphate (ALP), with no alternative explanation for the biochemical abnormality (i.e., without waiting for any additional etiologic investigations to have been concluded). AESIs will be identified via the AE form in the eCRF.

### 6.7.2 AEs of Special Monitoring

For rozanolixizumab, the following events are AESM that require immediate reporting (within 24 hours regardless of seriousness) to UCB:

- Severe and/or serious headache
- Suspected aseptic meningitis

AESMs will be identified via the AE form in the eCRF.

## 6.8 Appendix 8: AEs of focus

The following events are adverse events of focus for rozanolixizumab for all indications unless otherwise noted. Adverse events of focus will be listed for the ASPs. If there are any events, AEs of focus will be summarized for the SS.

**Table 6–1: AEs of focus**

Number	Event	Selection criteria
1	Headache	TEAE with HLGT='Headaches'
2	Possible aseptic meningitis	SMQ=' Noninfectious meningitis' narrow search

**Table 6–1: AEs of focus**

Number	Event	Selection criteria
3	Gastrointestinal disturbances	TEAE with HLT= ‘Gastrointestinal and abdominal pains (excl oral and throat)’ or HLT= ‘Nausea and vomiting symptoms’ or HLT= ‘Diarrhoea (excl infective)’ or HLT= ‘Gastritis (excl infective)’ or PT= ‘Abdominal discomfort’
4	Hypersensitivity reactions	SMQ = ‘Hypersensitivity’ narrow search
5	Anaphylactic reactions	<p>SMQ = ‘Anaphylactic reaction’ <u>and</u> TEAEs that either emerged on the <b>same day</b> as when a study medication injection reaction was received, or that emerged <b>one day after</b> a study medication injection was received, and which fulfill <u>any</u> of the following 3 criteria should be included in the summary table:</p> <ol style="list-style-type: none"> <li>1. If a subject reports any TEAE which codes to a PT included in Category A, then the event will be flagged as an anaphylactic reaction.</li> <li>2. If a subject reports any TEAE which codes to a PT included in Category B <b>AND</b> reports any TEAE which codes to a PT included in Category C, <b>and both TEAEs have the same start date</b>, then both events will be flagged as anaphylactic reactions.</li> <li>3. If a subject reports any TEAE which codes to a PT included in Category D <b>AND</b> reports (either a TEAE which codes to a PT included in Category B <b>OR</b> a TEAE which codes to a PT included in Category</li> </ol>

**Table 6–1: AEs of focus**

Number	Event	Selection criteria
		C), and both TEAEs have the same start date, then both events will be flagged as anaphylactic reactions.
6	Injection site reactions	TEAE with HLT='Injection site reactions' or HLT='Infusion site reactions' or HLT='Administration site reactions NEC'
7	Infections	TEAE with SOC = "Infections and infestations" <b>Note:</b> This was added as a reminder for safety that infections are considered as AE of focus and require assessment. No programming of this topic is required as TEAEs can be found in general AE Tables.
8	Opportunistic infections (Note: also included in AESM)	TEAEs in MedDRA SMQ = 'Opportunistic infections' narrow search
9	Reductions in albumin and plasma proteins (N/A in DB studies where values are blinded)	TEAEs with PT='Blood albumin decreased' or PT='Protein albumin ratio' or LLT='Plasma protein abnormal' or LLT='Proteins serum plasma low'
10	Effects on the kidney	TEAEs in SMQ= 'Acute renal failure' narrow search

**Table 6–1: AEs of focus**

Number	Event	Selection criteria
11	Drug related hepatic disorders	TEAEs in SMQ='Drug related hepatic disorders - comprehensive search' narrow and broad search
12	Effect on lipids	TEAEs with PT= 'Blood cholesterol increased' or PT= 'Low density lipoprotein increased' or PT= 'Blood triglycerides increased' or PT= 'Hypercholesterolaemia' or PT= 'Hypertriglyceridaemia' or PT= 'Hyperlipidaemia' or PT= 'Dyslipidaemia' or PT= 'Lipids increased'

## 6.9 Appendix 9: PK calculations

If calculable, pharmacokinetic parameters will be calculated by non-compartmental analysis methods from the concentration-time data following these guidelines:

- Actual time will be used in the calculation of all derived pharmacokinetic parameters.
- There will be no imputation of missing data.
- BLQ values at the beginning of a study participant profile (i.e., before the first incidence of a measurable concentration) will be assigned to zero. Embedded BLQ values (i.e., occurring between two measurable data points) and BLQ values occurring post- $C_{max}$  will be considered missing.

Pharmacokinetic parameters will be estimated according to the guidelines presented in [Table 6–2](#) below.

**Table 6–2: Pharmacokinetic Parameters and Estimation**

Parameter	Guideline for Derivation
$C_{max}$ , $t_{max}$	Obtained directly from the observed concentration-time data. Calculate for rozanolixizumab in breast milk and plasma
$Ae_{7d}$	Cumulative total amount excreted in milk to Day 7

**Table 6–2: Pharmacokinetic Parameters and Estimation**

Parameter	Guideline for Derivation
AUC <sub>(0-7d)</sub>	The AUC from zero time (pre-dose) to 144 h post dose will be calculated by a combination of the linear and logarithmic trapezoidal methods. Unless specifically requested and justified the linear up/log down trapezoidal method will be employed. Calculate for rozanolixizumab in breast milk and plasma.
Fe	$Ae_{7d}/\text{administered dose (mg)} \times 100 (\%)$
Milk:plasma AUC <sub>(0-7d)</sub> ratio	$AUC_{(0-7d)} \text{ in breast milk} / AUC_{(0-7d)} \text{ in maternal plasma} \times 100 (\%)$
Relative Infant Dose	$[(\text{Estimated}) \text{ Daily Infant Dosage (mg/kg/day)} / \text{Maternal Dosage (mg/kg/day)}] \times 100 (\%)$ (see Section 4.2.1.1 for details on the calculation of the estimated daily infant dosage)

## 6.10 Appendix 10: PK standard reporting procedures

### 6.10.1 PK concentrations

When reporting individual data in listings the following rules will apply:

- Concentrations below the limit of quantification should be reported as BLQ (below the limit of quantification).
- Concentrations should be listed to the same number of significant figures supplied by the bioanalytical laboratory.

When summarizing the data in tables the following rules will apply:

- To calculate descriptive statistics, BLQ values should be set to half the LLOQ value and missing values should be excluded.
- When the total number of BLQ and missing values exceeds one third of the total then only minimum and maximum should be reported for this timepoint. Other descriptive statistics should be reported as missing (“-“). The minimum should be reported as “BLQ”.
- When the mean value includes one or more replaced BLQ values then a footnote should be included to say “contains one or more BLQ value replaced by half the LLOQ value”
- A minimum of 3 values with at least 2/3 of the concentrations quantified are required to calculate summary statistics at the respective timepoint. If only 2 values are available then these should be presented as the minimum and maximum with other descriptive statistics reported as missing (“-“).
- If no participants have data, only n=0 will be presented. The other descriptive statistics will be left blank.
- Descriptive statistics will be reported to the same level of precision as the individual data for the minimum and maximum, and to 1 additional decimal place or 1 additional significant figure– depending on the reporting format of the original data with a maximum of 4

significant figures - for the mean (arithmetic and geometric), SD (arithmetic and geometric), CI, and median. Geometric CV will be reported as a percentage to 1 decimal place.

## 6.10.2 PK parameters

When reporting individual data in listings the following rules will apply:

- Individual PK parameters should be reported to 3 significant figures.
- If a parameter cannot be calculated, it should be reported as NE (not estimable i.e. if input data is missing which prevents calculation) or NC (not calculable i.e. if the data were available but the calculation was considered unreliable).

When summarizing the data in tables the following rules will apply:

- Descriptive statistics should be reported to 4 significant figures for the mean, SD, geometric mean, CI, and median and to 3 significant figures for the minimum and maximum. Geometric CV will be reported as a percentage to 1 decimal place.
- If at least two thirds of the study participants have a PK parameter reported then descriptive statistics will be calculated, otherwise only minimum and maximum will be reported for this PK parameter and all other descriptive statistics will be reported as NE (i.e. not estimable).
- A minimum of 3 values are required to calculate summary statistics. If only 2 values are available then these should be presented as the minimum and maximum with other descriptive statistics reported as missing (“-“)

## 6.11 Appendix 11: Laboratories Reporting Procedure

### 6.11.1 Laboratory Assessments Marked Abnormality Criteria for Adult Studies

The following criteria will be applied in the determination of marked abnormalities for laboratory assessment values. They are based on Version 5 of the Common Terminology Criteria for Adverse Events (CTCAE) grade 3 or higher criteria unless otherwise noted. If both high and low criteria are shown for a parameter, the criteria should be summarized separately in tabular data summaries.

**Table 6–3: Hematology**

Parameter	Unit (conventional)	Unit (standard)	Marked Abnormality Criteria
Hemoglobin	g/dL	g/L	<8.0 g/dL; <80 g/L
WBC (Leukocytes) <sup>1</sup>	10 <sup>9</sup> /L	10 <sup>9</sup> /L	Low: <2.0 x 10 <sup>9</sup> /L
			High: >30 x 10 <sup>9</sup> /L
Lymphocytes Absolute	10 <sup>9</sup> /L	10 <sup>9</sup> /L	Low: <0.5 x 10 <sup>9</sup> /L
			High: >20 x 10 <sup>9</sup> /L

**Table 6–3: Hematology**

Parameter	Unit (conventional)	Unit (standard)	Marked Abnormality Criteria
Neutrophils Absolute	10 <sup>9</sup> /L	10 <sup>9</sup> /L	<1.0 x 10 <sup>9</sup> /L
Platelets	10 <sup>9</sup> /L	10 <sup>9</sup> /L	<50.0 x 10 <sup>9</sup> /L

<sup>1</sup>WBC (Leukocytes) markedly abnormal high criterion is not based on Version 5 CTCAE Grade 3 or higher criteria. Due to the mechanism of action of rozanolixizumab, the safety alert is related to infection risk which would be identified by a lower cut-point than the standard which is related to acute leukemias. A markedly abnormal high cut-point >30 x 10<sup>9</sup>/L is applied to flag leukocytosis (George 2012).

**Table 6–4: Chemistry**

Parameter	Unit (conventional)	Unit (standard)	Marked Abnormality Criteria
AST (SGOT)	U/L	U/L	>5.0 x ULN
ALT (SGPT)	U/L	U/L	>5.0 x ULN
ALP (Alkaline Phosphatase)	U/L	U/L	>5.0 x ULN
GGT (Gamma Glutamyl Transferase)	U/L	U/L	>5.0 x ULN
Bilirubin (Total)	mg/dl	umol/L	>3.0 x ULN if Baseline value is normal; >3.0 x Baseline value if Baseline is abnormal
Albumin	g/dL	g/L	<2 g/dL; <20 g/L
Creatinine	mg/dl	umol/L	>3.0 x ULN or >3.0 x baseline
Estimate glomerular filtrate rate (eGFR) <sup>1</sup>	mL/min/1.73 m <sup>2</sup>	mL/min/1.73 m <sup>2</sup>	eGFR <29 mL/min/1.73 m <sup>2</sup>
C reactive protein (CRP) <sup>2</sup>	mg/L	mg/L	>100 mg/L
Calcium <sup>3</sup>	mg/dL	mmol/L	Low: Corrected serum calcium of <7.0 mg/dL; <1.75 mmol/L
			High: Corrected serum calcium of >12.5 mg/dL; >3.1 mmol/L

**Table 6–4: Chemistry**

Parameter	Unit (conventional)	Unit (standard)	Marked Abnormality Criteria
Immunoglobulin G <sup>4</sup>	(g/L)	(g/L)	≤1 g/L
Potassium	mmol/L	mmol/L	Low: <3.0 mmol/L
			High: >6.0 mmol/L
Sodium	mmol/L	mmol/L	Low: <125 mmol/L
			High: >155 mmol/L
Glucose <sup>5</sup>	mg/dL	mmol/L	Low: <40mg/dL; <2.2 mmol/L
			High: >250 mg/dL; >13.9 mmol/L
Total Cholesterol	mg/dL	mmol/L	>400 mg/dL; >10.34 mmol/L
Triglycerides	mg/dL	mmol/L	>500 mg/dL; >5.7 mmol/L

Abbreviations: ALT= alanine aminotransferase; AST = aspartate aminotransferase; dL = deciliter; GGT: gamma glutamyl transferase; L = liter; mg = milligram; mmol = millimoles; SGOT=serum glutamic-oxaloacetic transaminase; SGPT=serum glutamic-pyruvic transaminase; µg = microgram; U = unit; ULN = upper limit of normal

Note: Marked abnormality criteria are defined by Grade 3 or higher events according to the Common Terminology for Adverse Events (CTCAE), Version 5.0, unless otherwise noted.

<sup>1</sup>The value of eGFR is calculated using the Chronic Kidney Disease Epidemiology Collaboration or CKD-EPI formula ([https://qxmd.com/calculate/calculator\\_251/egfr-using-ckd-epi](https://qxmd.com/calculate/calculator_251/egfr-using-ckd-epi)) which is  $eGFR = 141 * \min(Scr/\kappa, 1)^\alpha * \max(Scr/\kappa, 1) - 1.209 * 0.993Age * 1.018$  [if female]; where Scr is serum creatinine (mg/dL),  $\kappa$  is 0.7 for females and 0.9 for males,  $\alpha$  is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/ $\kappa$  or 1, and max indicates the maximum of Scr/ $\kappa$  or 1. For derivation from values in standard units (umol/L) the  $\kappa$  values are 61.88 for females and 79.56 for males.

<sup>2</sup>Includes CRP and High Sensitivity (HS) CRP. Reference for marked abnormality criteria: Nehring, S.M.; Goyal, A.; Patel, B.C. (2020). StatPearls Publishing, web link: <https://www.ncbi.nlm.nih.gov/books/NBK441843/>. A moderate elevation of CRP level per referred reference is used for the marked abnormality criteria for RLZ to ensure a change suggestive of inflammatory process is captured. Standard CRP test should be used. In case high sensitivity CRP (hs-CRP) test have been used in any ongoing studies apply same value (>100mg/L) as marked abnormality criteria.

<sup>3</sup>Corrected Calcium (mmol/L) =  $0.02 * (40 - \text{Albumin (g/L)}) + \text{Calcium (mmol/L)}$ .

<sup>4</sup>Immunoglobulin G criterion based on immunodeficiency literature and noted in RLZ study protocols.

<sup>5</sup>Glucose high criterion defined by Grade 3 and higher events according to CTCAE, Version 4.03, June 14, 2010.

## 6.12 Appendix 12: Data disclosure reporting

The following tables outlined in previous sections fulfil the criteria for disclosure reporting for clinicaltrials.gov and EudraCT:

- DS\_T\_03 Disposition and Discontinuation Reasons [ASPS] as per Section 6.2
- DM\_T\_01 Demographics (all age categories are mandatory) [ASPS] as per Section 6.3
- AE\_T\_01 Incidence of TEAEs – Overview (mandatory, including both All Deaths and TEAE leading to Deaths)] [SS] as per Section 4.3.1

- AE\_T\_06 Incidence of Non-Serious TEAEs Above Reporting Threshold of X% of Participants [SS] as per Section 4.3.1
- DS\_T\_04 Discontinuation due to AEs\* [ASPS]
- AE\_T\_04b Incidence of serious TEAEs by Relationship\* [SS]
- AE\_T\_04b Incidence of fatal TEAEs by Relationship\* [SS]

\* For small studies in populations where these events are not expected then the study team may utilize the lines from AE\_T\_01. The zeros in the relevant lines are sufficient for the Clinical Trial Registry (CTR) reporting. However, if an event is observed then the relevant table must be produced by CTR reporting.

For results disclosure on public registries (e.g., ClinicalTrials.gov), TEAEs and treatment emergent SAEs will be published.

## 7 REFERENCES

CPMP/ICH/363/96. ICH E9 Expert Working Group. Note for Guidance on statistical principles for clinical trials: ICH Harmonised Tripartite Guideline. EMEA. 1998.

International Conference on Harmonisation: Statistical Principles for Clinical Trials (ICH E9)

International Conference on Harmonisation: Addendum on Estimands and Sensitivity Analysis in Clinical Trials to the Guideline on Statistical Principles for Clinical Trials (ICH E9 (R1))