STATISTICAL ANALYSIS PLAN

Study: UP0106

Product: Rozanolixizumab

A RANDOMIZED, PARTICIPANT-BLIND, INVESTIGATOR-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE SAFETY, TOLERABILITY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF ROZANOLIXIZUMAB ADMINISTERED SUBCUTANEOUSLY VIA MANUAL PUSH VERSUS SYRINGE DRIVER TO HEALTHY PARTICIPANTS

SHORT TITLE:

A Phase 1 study comparing the safety, tolerability, pharmacokinetics, and pharmacodynamics of subcutaneous rozanolixizumab administered via manual push vs syringe driver to healthy participants

Sponsor Name: UCB Pharma SRL

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Regulatory Agency Identifier Number(s):

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SAP-Amendment Number	Date
Final Version 1.0	**06 May 2021**
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Final Version 2.0 / Amendment 1	**1 December 2021**

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VERSION HISTORY

SAP Version	Approval Date	Change	Rationale
1.0	06 May 2021	Not Applicable	Original version
2.0	17 August 2021	Updates following protocol amendment v2.0 and updates following the release of the AE of focus guideline (v2.0 dated 24 June 2021). Updates to ensure consistency in the Rozanolixizumab program with regards to classification of concomitant medication and duration of Adverse Events	Protocol Amendment
2.0 Amendment 1	1 December 2021	Updating the reference ranges for Serum Calcium and the eGFR calculation	Change in reference ranges for the clinical program

LIST OF ABBREVIATIONS

List of Abbreviations

ADA	antidrug antibody
AEOF	adverse event of focus
ANOVA	analysis of variance
AUC	area under the concentration-time curve
$AUC_{(0-t)}$	area under the concentration-time curve from 0 to time t
AE	adverse event
AESI	adverse event of special interest
ALP	alkaline phosphatase
ALQ	above the limit of quantification
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BLQ	below the limit of quantification
BMI	body mass index
BP	blood pressure
C_{max}	maximum plasma concentration
COVID-19	coronavirus disease-19
CI	confidence interval
CRO	contract research organization
CSR	clinical study report
CV	coefficient of variation
DEM	data evaluation meeting
ECG	electrocardiogram
eCRF	electronic case report form
EudraCT	European Union Drug Regulating Authorities Clinical Trials
ES	Enrolled Set
FDA	US Food and Drug Administration
GLSM	geometric least square mean
GLSMR	geometric least square mean ratio

List of Abbreviations

HLT	high level term
ICF	informed consent form
ICH	International Council for Harmonisation
IgG	immunoglobulin G
IMP	investigational medicinal product
IPD	important protocol deviation
ISRQ	injection site reaction questionnaire
LLOQ	lower limit of quantification
LSM	least square mean
MedDRA	Medical Dictionary for Regulatory Activities
MP	manual push
MRD	minimum required dilution
MSR	minimum significant ratio
PCR	polymerase chain reaction
PCS	potentially clinically significant
PD	pharmacodynamic
PD-PPS	Pharmacodynamic Per Protocol Set
PDILI	potential drug-induced liver injury
PK	pharmacokinetic
PK-PPS	Pharmacokinetic Per Protocol Set
PT	preferred term
QTcF	QT corrected for heart rate using Fridericia's formula
R_{min}	maximum decrease in total plasma IgG
RS	Randomized Set
SAE	serious adverse events
SAP	Statistical Analysis Plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SC	subcutaneous(ly)
SD	standard deviation

List of Abbreviations

SFU	Safety Follow-up
SIAQ	self-injection assessment questionnaire
SMC	safety monitoring committee
SOC	system organ class
SS	Safety Analysis Set
TEAE	treatment-emergent adverse event
TEMA	treatment-emergent markedly abnormal
TFLs	tables, figures, and listings
t_{max}	time to maximum plasma concentration
t_{min}	time to maximum plasma concentration
ULN	upper limit of normal
VAS	visual analog scale
WHODD	World Health Organization Drug Dictionary

1 INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to provide all information that is necessary to perform the required statistical analysis of study UP0106. It also defines the summary tables figures, and listings (TFLs) to be included in the final clinical study report (CSR) according to the protocol.

This SAP is based on, and assumes familiarity, with the following documents:

- Protocol version- amendment 2, dated 03 June 2021.
- electronic Case Report Form (eCRF) version 3.0, dated 26 May 2021.

Unless specified in the sections below, the study will be analyzed as described in the most recent version of the protocol.

If a future protocol amendment necessitates a substantial change to the statistical analysis of the study data, this SAP will be updated accordingly. If, after database lock, additional analyses are required to supplement the planned analyses described in this SAP, those unplanned analyses will be described in a separate analysis plan. However, if analysis definitions have to be modified or updated prior to database lock, a further SAP amendment will be required.

The content of this SAP is compatible with the International Council for Harmonisation (ICH)/US Food and Drug Administration (FDA) E9 Guidance documents.

UCB is the Sponsor and ICON is the Contract Research Organization (CRO) for this study.

1.1 Objectives and Estimands/Endpoints

The study objectives and endpoints are presented in Table 1-1.

Table 1-1: Study objectives and endpoints

Objectives	Endpoints/Estimands
Primary	
• To evaluate the safety and tolerability of a [redacted] SC dose of rozanolixizumab administered to healthy participants by manual push (MP) vs syringe driver	• Incidence of TEAEs
Secondary	
• To assess the PK and PD of a [redacted] SC dose of rozanolixizumab administered by MP vs syringe driver	• PK endpoints: • C_{max}, t_{max}, $AUC_{(0-t)}$ • PD endpoints: • Baseline-corrected area under the Total IgG-time curve • R_{min} • t_{min}
Exploratory	
• To compare the PK and PD of a [redacted] SC dose of rozanolixizumab administered by MP vs syringe driver	• PK comparisons: C_{max}, $AUC_{(0-t)}$ • PD comparison: Baseline-corrected Total IgG AUC
• To evaluate the immunogenicity of rozanolixizumab following SC administration	• Anti-rozanolixizumab antibody screening status (positive or negative screen), confirmatory status (positive or negative immunodepletion), and the titer for "positive immunodepletion" samples at each scheduled assessment during the In-Clinic and SFU Periods
• To evaluate the effects of rozanolixizumab on the concentrations of IgG on tetanus, influenza A virus-specific IgG antibody, and COVID-19 vaccinated/previously infected participants	• Values and change from Baseline in serum IgG concentrations at each scheduled assessment during the In-Clinic and SFU Periods • Values and change from Baseline in tetanus, influenza A virus-specific IgG antibodies, and COVID-19 vaccinated/previously infected

Table 1-1: Study objectives and endpoints

Objectives	Endpoints/Estimands
	participants during the In-Clinic and SFU Periods
• To assess total volume, total time, and infusion rate for MP and syringe driver	• Volume of IMP administration • Time from start to completion and resultant infusion rate of IMP administration • Time of infusion setup for both modes of administration
• To assess acceptability of SC rozanolixizumab administration by MP vs syringe driver	• Post-dose infusion site pain visual analog scale with IMP administration
• To assess the experience with SC infusions	• Pre- and post-dose SIAQ for MP administration • Post-dose ISRQ for syringe driver administration
Other Safety	
• To evaluate changes from Baseline in vital signs, 12-lead electrocardiogram, and laboratory measurements following [redacted] doses of rozanolixizumab administered by SC MP vs syringe driver in healthy study participants	• Vital signs measurements (blood pressure, pulse rate, respiratory rate, and body temperature), 12-lead electrocardiogram, and local tolerability assessments at each scheduled assessment during the In-Clinic and SFU Periods • Changes from Baseline in clinical laboratory assessments will consist of hematology including coagulation, clinical chemistry, and urinalysis at each scheduled assessment during the In-Clinic and SFU Periods
• To further evaluate the safety and tolerability of a [redacted] SC dose of rozanolixizumab administered to healthy participants by MP vs syringe driver	• Occurrence of serious TEAEs • Occurrence of treatment-related TEAEs • Occurrence of TEAEs leading to withdrawal • Occurrence of AEs of special monitoring • Comparison of TEAEs for MP vs syringe driver • Serum complement (C3, C4), and cytokines and plasma complement (C3a, C5a)

AE=adverse event; AUC=area under the concentration-time curve; $AUC_{(0-t)}$=area under the concentration-time curve from 0 to time t; C_{max}=maximum plasma concentration; COVID-19=coronavirus disease-19; IgG=immunoglobulin G; IMP=investigational medicinal product; MP=manual push; ISRQ=injection site reaction questionnaire; PD=pharmacodynamic(s); PK=pharmacokinetic(s); R_{min}=maximum decrease in total plasma IgG; SC=subcutaneous(ly); SFU=Safety Follow-Up; SIAQ=self-injection assessment questionnaire;

TEAE=treatment-emergent adverse event; t_{max}=time to maximum plasma concentration; t_{min}=time to minimum IgG level.

1.2 Study design

This Phase 1 study is a randomized, participant-blind, investigator-blind, placebo-controlled safety/tolerability, pharmacokinetic (PK), and pharmacodynamic (PD) evaluation of a [redacted] rozanolixizumab subcutaneous (SC) dose administered to healthy participants by either a programmed syringe driver or by manual push (MP) via self-administration. As rozanolixizumab has not been administered SC to humans by MP, this study represents a preliminary assessment of the MP method prior to recommendation of this administration technique in the clinical dosing of rozanolixizumab.

Participants are divided into 2 body weight categories: ≥35 to <50kg and ≥50kg. Within the higher body weight category, 16 participants were to be randomly allocated to syringe driver or MP cohorts and, subsequently, to rozanolixizumab (6 participants total) or placebo (2 participants total) (Figure 1-1). Participants of lighter body weights between ≥35 to <50kg are being investigated to a) support the newly recommended rozanolixizumab dosing with a fixed dose of [redacted] in adults of ≥35kg to 50kg (via syringe driver administration) and (b) to assess the MP method for a [redacted] dose) investigational medicinal product (IMP) volume.

Within the lower body weight category, the allocation to either syringe driver or MP was to be determined by order of recruitment rather than randomization. The first 8 participants were to be allocated to the syringe driver cohort and randomly allocated to receive either rozanolixizumab [redacted] (6 participants total) or placebo (2 participants total). The subsequent 8 participants were to be allocated to the MP cohort and randomly allocated to receive either rozanolixizumab [redacted] (6 participants total) or placebo (2 participants total).

The treatment groups were planned as follows:

- Cohort 1 (participants with a body weight of ≥35kg to <50kg) was planned to have 6 participants receive rozanolixizumab [redacted] and 2 participants receive placebo via syringe driver at a [redacted].
- Cohort 2 (participants with a body weight of ≥35kg to <50kg) was planned to have 6 participants receive rozanolixizumab [redacted] and 2 participants receive placebo via MP through self-administration at a [redacted].
- Cohort 3 (participants with a body weight of ≥50kg) was planned to have 6 participants receive rozanolixizumab [redacted] and 2 participants receive placebo via syringe driver at a [redacted].
- Cohort 4 (participants with a body weight of ≥50kg) was planned to have 6 participants receive rozanolixizumab [redacted] and 2 participants receive placebo via MP through self-administration at a [redacted].

Since a [redacted] rozanolixizumab fixed dose has not been investigated thus far in lower weight (35 to 50kg) healthy participants, 2 sentinel study participants (1 active + 1 placebo) were to be incorporated into Cohort 1 in order to collect safety and tolerability data over a 72-hour period. The safety monitoring committee (SMC) is to convene to evaluate all available safety and tolerability data following completion of a 72-hour evaluation period and prior to staggered dosing

of remaining participants in Cohort 1. As a further precautionary step for Cohort 1, dosing of the 6 post-sentinel participants was to be staggered such that no more than 2 participants were to be dosed in a 72-hour period with a minimum of 48 hours between participants. In addition, the Rapid Alert process is in place throughout the study to ensure that exposure to the study medication is stopped if a reported event meets the stopping criteria (see protocol Appendix 8 [Section 10.8]). Cohorts are not obliged to run in numerical sequence (i.e., cohorts could run in parallel).

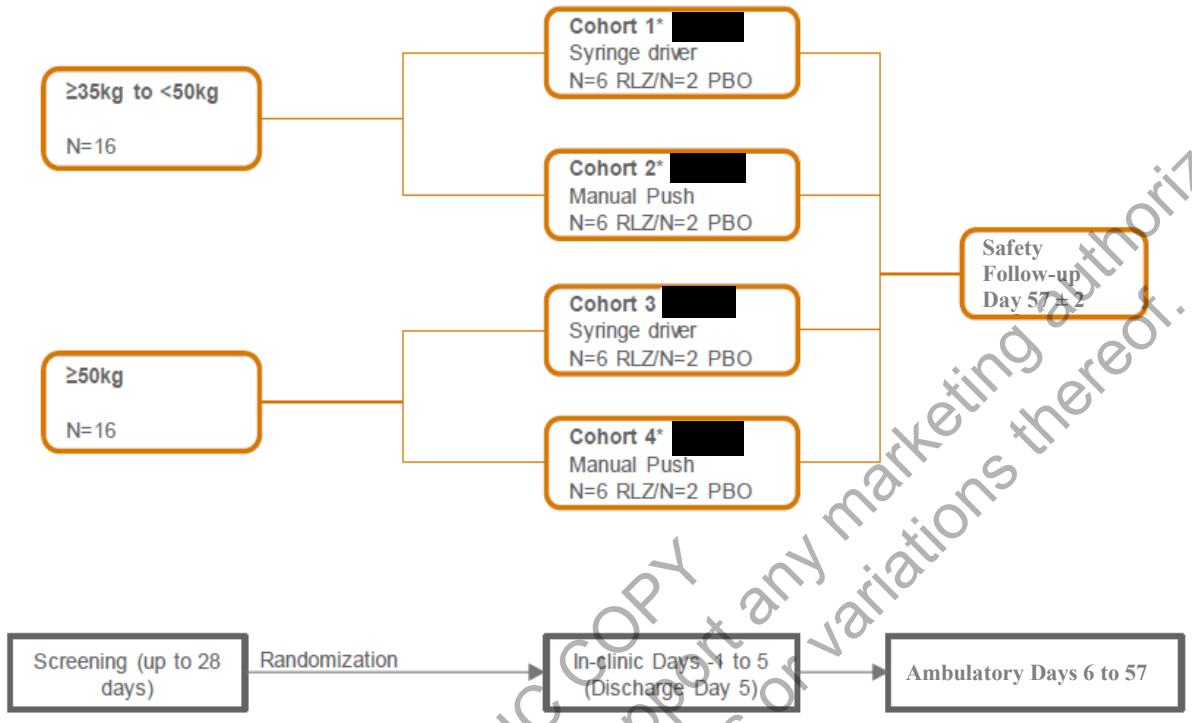
The eligibility of study participants is determined during a Screening Period of up to 4 weeks (Day -28 to Day -2). Once eligibility is confirmed, the study participant was to be admitted to the site (at Day -1 or the evening of Day -2) and will enter an In-Clinic Period through Day 5. Each study participant will receive a [redacted] SC dose of rozanolixizumab on Day 1 and may be discharged beginning at Day 5 at the discretion of the investigator. Each participant will only receive [redacted] IMP administration.

Beginning at Day 6, study participants will enter the Ambulatory Period and will attend the clinical site for study visits through Day 57 to allow sufficient time for systemic immunoglobulin G (IgG) levels to return to Baseline and for the assessment of anti-drug antibodies (ADAs).

The total maximum study duration per study participant is up to 12 weeks. This includes a 4-week Screening Period, 5-day In-Clinic Period, and the Ambulatory Period from Day 7 through Day 57.

Photographs of the infusion site will be taken, without participant personal or facial identification, for all participants prior to start and 30 minutes after the end of the IMP administration, and additionally upon occurrence of any injection site reaction.

Figure 1-1: Study schematic



2 STATISTICAL HYPOTHESES

Not applicable, there is no hypothesis testing in the study.

3 SAMPLE SIZE DETERMINATION

No formal statistical sample size calculation has been performed as this study constitutes a preliminary assessment of SC rozanolixizumab delivery by MP. The primary objective of the study is to evaluate the safety and tolerability of a [redacted] SC dose of rozanolixizumab administered to healthy participants by MP vs syringe driver. A total sample size of approximately 32 participants randomly assigned to study medication resulting in at least 6 evaluable participants per cohort is considered sufficient to meet the primary objective.

4 POPULATIONS FOR ANALYSIS

Enrolled Set: The Enrolled Set (ES) will consist of all study participants who have signed the Informed Consent Form (ICF).

Randomized Set: The Randomized Set (RS) consist of all enrolled study participants who were randomized.

Safety Analysis Set (SS): All randomized study participants who received IMP. Analysis of this set will be according to the treatment the study participants actually received and will be used for the demographic and safety analyses.

Pharmacokinetic (PK) Per Protocol Set (PK-PPS): All study participants that received active study medication and had at least 1 observable PK measurement and had no important protocol deviations affecting the PK parameters. If a study participant in the PK-PPS is missing individual time points or are otherwise unobservable, they will be included in the PK-PPS but those time points will be omitted from the PK summaries, as appropriate.

Pharmacodynamic (PD) Per Protocol Set (PD-PPS): The PD-PPS is a subset of the SS, consisting of those study participants who had no important protocol deviations affecting the PD variables, as confirmed during a pre-analysis review of the data prior to database lock.

5 STATISTICAL ANALYSES

5.1 General Considerations

This is a Phase 1 study to evaluate the safety and tolerability of a [redacted] SC dose of rozanolixizumab administered to healthy participants by MP vs syringe driver.

Statistical evaluation will be performed by UCB or designee with oversight by the Statistical Sciences and Innovation Department of UCB. All analyses will be performed using SAS® version 9.4 or later (SAS Institute, Cary, NC, USA).

Missing data will not be imputed. Outlier detection and statistical analysis of outliers will not be performed. Unless otherwise stated, Baseline will be the last non-missing data collected prior to the IMP administration (refer Section 5.1.1.1.4).

Continuous variables will be summarized by cohort and in each cohort by treatment groups rozanolixizumab [redacted] or placebo, and day (where applicable); with statistics including, the number of study participants, mean, standard deviation (SD), interquartile range, median, minimum, maximum, and 95% confidence interval (CI), if applicable. Categorical variables will be summarized by cohort, treatment group, and day (where applicable) with frequency counts and percentages. Coefficient of variation (CV) and geometric mean will be used for PK parameters.

In addition, the results will be summarized by administration method (manual push or syringe driver), and within administration method, by treatment group (rozanolixizumab, regardless of dose, or placebo).

When reporting relative frequencies or other percentage values, the following rules apply:

- For values where all participants fulfill certain criteria, the percentage value will be displayed as 100
- For values where the absolute frequency is zero, there will be no percentage displayed at all
- All other percentage displays will use 1 decimal place

- Percentages displayed based on continuous data (eg, percentage changes from Baseline) will be displayed to 1 decimal place eg, 100.0 and 0.0.
- Unless otherwise stated, the percentages will be based on the number of participants in the respective analysis population and treatment group.

When reporting descriptive statistics, the following rules will apply in general:

- "n" will be an integer.
- Mean (arithmetic and geometric), 95% CI, SD, and median will use 1 additional decimal place compared to the original data.
- Coefficient of variance (CV [%]) will be presented with 1 decimal place.
- Minimum and maximum will have the same number of decimal places as the original value.
- If no participants have data at a given time point, then only n=0 will be presented. If n<3, only the n, minimum, and maximum will be presented. If n=3, only the n, median, minimum, and maximum will be presented. The other descriptive statistics will be left blank.

When reporting descriptive statistics for PK data, the following rules will apply with regard to rounding and precision:

- Individual values for PK concentration data will be reported to the same level of precision as received from the bioanalytical laboratory.
- Descriptive statistics for PK concentration data will be reported to the same level of precision as the individual data for the minimum and maximum, and to 1 additional significant figure for the mean (arithmetic and geometric), median, SD, and 95% CI for the geometric mean.
- Individual values for PK parameters will be reported to 3 significant figures.
- Descriptive statistics for PK parameters will be reported to 3 significant figures for minimum and maximum and to 4 significant figures for the mean (arithmetic and geometric), median, SD, and 95% CI for the geometric mean.
- Geometric CV will be reported as a percentage to 1 decimal place.
- 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 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 ("-").

Additional rules regarding handling of values that are BLQ are presented in Section 6.1.5.2.

5.1.1 General study level definitions

5.1.1.1 Analysis Time Points

5.1.1.1.1 Relative day

The relative day of an event will be derived with the date of dosing as reference. Relative days for an event or measurement occurring before the date of dosing are calculated as follows:

Relative Day = [(Event Date – Date of Dosing)]

The relative day for an event or measurement occurring on the date of dosing is 1 and is calculated as follows:

Relative Day = [(Event Date – Date of Dosing) + 1]

For events or measurements occurring after the date of dosing, relative day will be prefixed with '+' in the data listings and will be calculated as follows:

Relative Day = + [(Event Date – Date of Dosing)]

There is no relative Day 0. Relative day is not calculated for partial dates in cases where relative day is shown in a participant data listing. In such cases, relative day should be presented as '--' in the relevant listing.

5.1.1.1.2 Study periods

The following study periods are defined:

Pre-treatment Period: This period is defined as the period prior to the date of first dose of IMP. The period ends at the day prior to the date of IMP administration.

In-Clinic Period: This periods starts at the date of first dose of IMP (Day 1) and ends on the date of discharged from the clinical study center (Day 5).

Ambulatory Safety Follow-Up Period: This period starts at the day after the date of discharge (Day 5) and ends at study completion(i.e. Day 6 through Day 57).

5.1.1.1.3 Mapping of assessments performed at Early Discontinuation Visit

Participants who withdraw from the study will be encouraged to return to the clinic to complete the Withdrawal Visit.

The following rules will apply regarding the inclusion of data obtained at the early discontinuation visit in the summaries and in the data listings:

- If the early discontinuation occurs at the time of the next scheduled visit, the results will be included with all other participants' results from that visit.
- If the early discontinuation visit does not correspond to the day of a scheduled visit, the results will be mapped to the nearest scheduled visit following the last scheduled visit where assessments were performed.

- If the date of the early discontinuation visit is equidistant between 2 scheduled visits at which no scheduled assessments were performed, the results from the withdrawal visit will be mapped to the earliest of these visits.

The results from the early discontinuation visit will be displayed as the mapped visit and will be flagged in the data listings.

5.1.1.1.4 Definition of Baseline values

In general, Baseline will be the last non-missing value prior to dosing. Scheduled or unscheduled measurements can be used as the Baseline value.

5.1.1.2 Protocol Deviations

Important protocol deviations are deviations from the protocol which potentially could have a meaningful impact on study conduct, or on the PK, PD and key safety for an individual study participant. The criteria for identifying important protocol deviations will be defined within the appropriate protocol-specific document. Important protocol deviations will be reviewed as part of the data cleaning process and all important deviations will be identified and documented before unblinding to confirm exclusion from analysis sets.

After all data have been verified/coded/entered into the database, a blinded data review will be performed prior to database lock, at a Data Evaluation Meeting (DEM). The purpose of this review meeting will be to examine all protocol deviations, define the PK-PPS and PD-PPS, and to verify the quality of the data. The data evaluation will also help in guiding decisions on how to manage data issues on a case by case basis (e.g., missing values, dropouts, and protocol deviations). Protocol deviations (e.g., missing assessments or visits) related to coronavirus disease-19 (COVID-19) will be listed separately and will be reviewed for the definition of the PK-PPS and PD-PPS analysis sets.

All Important Protocol Deviations (IPDs) will be discussed and documented at the DEM together with any decisions regarding exclusion from analysis sets. If necessary, appropriate actions will be implemented in the SAP amendment before locking the database. After the DEM, resolution of all issues, and documentation of all decisions, the database will be locked.

5.1.1.3 Treatment assignment and treatment groups

Treatment assignment for the SS, PK-PPS and PD-PPS will be according to the actual treatment received. Listings and summaries will be presented by cohort and treatment group.

The following label conventions and order will be used in the TFLs (except for PK analysis)

- Cohort 1 - ≥35kg to <50kg, Syringe driver
  - Placebo via Syringe Driver
  - Rozanolixizumab [redacted] Syringe Driver
- Cohort 2 - ≥35kg to <50kg, MP

- Placebo via MP
- Rozanolixizumab [redacted] MP

- Cohort 3 -≥50kg, Syringe driver
  - Placebo via Syringe Driver
  - Rozanolixizumab [redacted] Syringe Driver
- Cohort 4 -≥50kg, MP
  - Placebo via MP
  - Rozanolixizumab [redacted] MP
- Syringe Driver, All Participants
  o Placebo
  o Rozanolixizumab
- MP, All Participants
  o Placebo
  o Rozanolixizumab

The following label conventions and order will be used in the PK TFLs:

- Rozanolixizumab via Syringe Driver, All
- Rozanolixizumab via MP, All

The explanatory description of each cohort may be dropped from the labels if space is limited. For listings, the cohort description and the treatment name will be written out in full.

5.1.1.4 Center pooling strategy

Not applicable, this is a single center study.

5.1.1.5 Coding dictionaries

Adverse events and medical history will be coded using Version 23.1 of the Medical Dictionary for Regulatory Activities (MedDRA®). Medications will be coded according to the World Health Organization Drug Dictionary (WHODD). Medical procedures will not be coded.

5.1.1.6 Multicenter studies

This is a single center trial, therefore this section is not applicable.

5.2 Participant Disposition

The number of participants who were enrolled, randomized into the study, included in each analysis set, and completed or prematurely discontinued from the study, as well as the reason for discontinuation, will be summarized by cohort and treatment group.

Screen failure reasons will be summarized based on the ES.

In addition, the following listings will be presented by cohort and treatment group:

- Participant disposition (ES)
- Participant analysis sets (ES)
- Participant discontinuing from the study (RS)
- Study visit dates (RS)

The listing of participants disposition will include the date of informed consent, date of randomization, date and time of dosing, date of premature study termination, primary reason for premature discontinuation (if applicable), date of final contact, and date of premature unblinding and reason for code break (if applicable).

The listing of study discontinuation will include the reason for discontinuation and the number of days since dosing.

The number and percentage of study participants who discontinued due to adverse events (AEs) will be summarized separately by cohort and treatment group, based on the randomized participants. This will be used for European Union Drug Regulating Authorities Clinical Trials (EudraCT) reporting.

5.3 Primary Endpoint(s) Analysis

The primary endpoint is:

- Incidence of Treatment-emergent adverse event (TEAE).

5.3.1 Definition of endpoint(s)

A TEAE is defined as any AE with a start date/time on or after first dose of study medication until 8 weeks after dosing of study medication (termination or withdrawal visit) .

5.3.2 Main analytical approach

All AEs and serious adverse events (SAEs) will be collected from the signing of the ICF until the Safety Follow-up/Withdrawal Visit. All AEs will be coded (Section 5.1.1.5) and categorized by intensity (mild/moderate/severe) and relationship to study drug (related/not related). Only TEAEs will be included in the summary tables and listings.

The number and percentage of participants who experience TEAEs will be summarized by cohort, treatment group, system organ class (SOC) and preferred term (PT) based on the safety analysis set. Summaries of TEAEs will include the following:

- Overview of TEAEs (overview including number and percentage of participants with any TEAEs, serious TEAEs, discontinuations due to TEAEs, drug-related TEAEs, severe TEAEs, TEAEs of special interest and TEAEs leading to death; event counts will also be included)
- Incidence of TEAEs
- Incidence of TEAEs leading to study medication interruption
- Incidence of serious TEAEs
- Incidence of non-serious TEAEs
- Incidence of TEAEs by relationship to study medication
- Incidence of TEAEs by maximum relationship to study medication
- Incidence of TEAEs by intensity
- Incidence of TEAEs by maximum intensity
- Incidence of non-serious TEAEs by relationship
- Incidence of serious TEAEs by relationship
- Incidence TEAEs of special interest
- Incidence of TEAEs of Focus (see Appendix 6.1.8)
- Incidence of TEAEs of special monitoring
- Incidence of TEAEs by TE ADA status

In case of missing or incomplete dates, AEs will be assumed to be treatment-emergent and will be handled as described in Section 6.1.5.3.

Summary tables will contain counts of participants, percentages of participants (in parentheses), and the number of events where applicable. A participant who has multiple events in the same SOC and PT will be counted only once in the participant counts but all events will be included.

In summaries including relationship, the following relationships will be summarized: ‘not related’, ‘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.

Adverse event summaries will be ordered alphabetically by SOC and decreasing frequency of PT within SOC in the ”Rozanolixizumab” cohort 1 column for tables including event counts. For tables including only number and percentage of participants, summaries will be ordered alphabetically by SOC and decreasing incidence of PT within SOC in the “Rozanolixizumab” column.

A listing will be presented by treatment group for all AEs and will include the onset date/time and outcome date/time of the event (including relative days), the AE duration (derived), pattern of event, intensity, relationship, action taken and outcome. In addition, the listing will flag AEs that led to discontinuation, TEAEs, and SAEs.

5.3.3 Sensitivity analysis

No sensitivity analysis is planned for this study.

5.3.4 Supplementary analyses

No supplementary analysis is planned for this study.

5.4 Secondary Endpoint(s) Analysis

5.4.1 Key/Confirmatory secondary endpoint(s)

PK endpoints

- Maximum plasma concentration (C_{max})
- Time to maximum plasma concentration (t_{max})
- Area under the concentration-time curve from 0 to time t ($AUC_{(0-t)}$)

PD endpoints:

- Baseline-corrected area under the Total IgG-time curve
- Maximum decrease in total plasma IgG (R_{min})
- Time to minimum IgG level (t_{min})
- Total IgG

5.4.1.1 Definition of endpoint(s)

Pharmacokinetics will be determined by non-compartmental analysis in Phoenix WinNonlin (Certara, USA) using the PK Per Protocol Set.

For calculation of the plasma PK parameters of rozanolixizumab, the actual sampling time points along with the actual dose administered and duration of administration will be used in order to evaluate the PK parameters.

Venous blood samples will be collected at protocol specified time points for the measurement of Total IgG.

5.4.1.2 Main analytical approach

PK analyses

All PK summaries will be done using PK-PPS and displayed by method of administration (see section 5.1.1.3). The plasma concentration-time profiles and PK parameters of rozanolixizumab (C_max, AUC, and T_max) will be summarized by method, dose and body weight for rozanolixizumab treated patients using descriptive statistics (number of available observations, arithmetic mean, standard deviation, the geometric mean, the coefficient of variation of the geometric mean, median, minimum, and maximum). For tmax , only median, minimum and maximum will be reported. Values below LLOQ will be reported with a clear sign indicating that they were below the LLOQ. Descriptive statistics of concentrations will be calculated if at least two-thirds of the individual data points are quantifiable (≥LLOQ).

Individual and spaghetti concentration time profiles will be displayed graphically on a linear-linear scale and semi-logarithmic scale. Geometric mean plasma concentrations-time curves including 95% CI will be displayed.

The comparability of dose-adjusted PK parameters (C_{max}/D and $AUC_{(0-t)}$/D) between the methods (MP and the syringe driver) will be assessed within an analysis of variance (ANOVA) model with method (MP vs syringe driver) as a main effect, with no additional covariates. The log-transformed PK parameters will be used in the ANOVA model. The model structure to be used is therefore

$$\log(Parameter) \sim Method\ of\ Administration$$

This model structure has been chosen to reflect the intended dosing scheme of fixed dosing (e.g., of [redacted]) applied to adults >35kg irrespective of weight. This will thus allow us to draw conclusions about the presence or absence of effects of the method of dose administration on parameter values when given using the intended scheme. Any potential effect of weight on parameter values will be accounted for by the study design itself by the balanced proportion of lower weight/higher weight participants receiving their dose using each of MP and Syringe driver.

The geometric least square mean (GLSM), GLSM differences and the corresponding 90% CI for the differences (MP [Test] - syringe driver [Reference]) will be calculated for PK parameters (log-transformed C_{max}, AUC_{0-t}). Back-transformed (anti-log) estimates of (GLSM, geometric least square mean ratio (GLSMR) and its 90% CI for the comparisons will be presented. In order to verify the normality assumption of the ANOVA, normal quantile-quantile plots will be used to visually inspect the distribution of residuals, and the potential impact of any deviations will be discussed.

PD analyses

All PD summaries will be done using PD-PPS by treatment group described under section 5.1.1.3. Total IgG (observed values, change from Baseline, and percentage change from Baseline) will be listed and summarized for the PD Per Protocol Set. The geometric mean Total IgG concentration with 95% CI will be displayed graphically.

Derived parameters for the Total IgG response curve (AUC, maximum decrease in total plasma IgG, and time to minimum plasma concentration) will be listed and summarized for the PD Per Protocol Set.

The comparability of the total dose adjusted IgG Baseline-corrected AUC (IgG)/D between MP and the syringe driver will be assessed within an ANCOVA model with Baseline IgG value fitted as a covariate. The least square mean (LSM), LSM differences and the corresponding 95% CI for

the differences will be presented for total IgG. The analysis may be conducted on the log scale if the data exhibits substantial non-normality. In this case, the reason for the log-transformation will be described.

The following contrasts will be presented:

- Rozanolixizumab via Syringe Driver vs Rozanoliximab via MP
- Placebo via Syringe Driver vs Placebo via MP
- Rozanolixizumab via Syringe Driver vs Placebo via Syringe Driver
- Rozanoliximab via MP vs Placebo via MP

Additionally, observed values and change from Baseline in serum IgG concentrations at each scheduled assessment during the In-Clinic and SFU Periods will be summarized descriptively.

5.4.2 Supportive secondary endpoint(s)

Not applicable no supportive secondary analysis is planned for this study.

5.5 Exploratory Endpoint(s) Analysis

Exploratory endpoints related to the comparison of PK and PD parameters are covered under section 5.4.

5.5.1 Immunogenicity Analyses

The development of antidrug antibodies during the study will be evaluated to assess the immunogenicity potential of the study drug.

The anti-drug (rozanolixizumab) antibody (ADA) screening status (positive or negative screen), confirmatory status (positive or negative immunodepletion), and the titer for "positive immunodepletion" samples at each scheduled assessment during the In-Clinic and SFU Periods will be presented.

The results of the ADA analyses will be listed and summarized by cohort treatment group (refer section 5.1.1.3) and time point for the SS.

Anti-drug antibodies will be measured using a three-tiered assay approach: screening assay, confirmatory assay and titration assay. All immunological analyses will be exploratory.

Samples will first be evaluated in the screening assay using a false positivity rate of 5% (reported as 'negative screen' or 'positive screen'), followed by analysis of screened positive samples in the confirmatory assay (which is a drug depletion assay) to confirm the true positivity of the samples (reported as 'negative immunodepletion' or 'positive immunodepletion'). Samples that are confirmed as positive will be evaluated in a titration assay to quantify the ADA level and will be reported as titer (reciprocal dilution factor including minimum required dilution (MRD)).

The ADA status should be determined for each visit where samples were taken for ADA analysis.

- Sample values that are either 'negative screen' or 'positive screen' and 'negative immune depletion' will be defined as ADA negative.
- Sample values that are 'positive screen' and 'positive immune depletion' will be defined as ADA positive.

In addition, the anti-drug antibody status will be further classified based on participant levels as outlined below. This classification should be done for entire study duration (i.e. the treatment period including SFU sampling time point).

1. **Pre ADA negative – treatment induced ADA negative**: Includes participants who are negative at Baseline and antibody negative at all sampling points post treatment. This group also includes participants who have a missing pretreatment sample (either missing or insufficient volume) at Baseline with all ADA post-treatment samples negative.
2. **Pre ADA negative – treatment induced ADA positive**: Includes participants who are negative at Baseline and antibody positive at any sampling point post treatment. This group also includes participants who have a missing pretreatment sample (either missing or insufficient volume) at Baseline with one or more ADA positive post-treatment samples.
3. **Pre ADA positive – treatment reduced ADA**: Includes participants who are positive at Baseline, and antibody negative at all sampling points post treatment.
4. **Pre ADA positive – treatment unaffected ADA**: Includes participants who are positive at Baseline and are positive at any sampling point post treatment with titer values of the same magnitude as Baseline (ie, less than a predefined fold difference increase from the Baseline value, i.e. the minimum significant ratio (MSR) determined during assay validation).
5. **Pre ADA positive – treatment boosted ADA positive**: Includes participants who are positive at Baseline and are positive at any sampling point post treatment with increased titer values compared to Baseline (greater than a predefined fold difference increase from Baseline value, i.e. the MSR determined during assay validation).
6. **Inconclusive**: Includes participants who have a positive or negative pretreatment sample and at least one post-treatment samples are missing, while other post-treatment samples are ADA negative.

Based on the overall ADA participant classification above, the following will be determined and presented in tables:

- Total prevalence of pre-Antibody: n/N % number of participants that are pre ADA positive, i.e. from categories 3, 4, 5.
- Total incidence of treatment-emergent ADA positive: n/N % number of participants in category 2 and category 5.

The following summaries, figures and listings will be produced and will be presented:

- Summary table displaying the number and percentage of participants with a positive ADA status and negative ADA at the time of each visit by cohort and treatment group.
- Summary tables displaying the number and percentage of participant in each of the ADA participant categories (1 – 6), total prevalence of pre-Antibody and total incidence of treatment-emergent ADA positivity as defined above by cohort treatment group.

Spaghetti plots of ADA titer (y-axis) by visit (x-axis). This plot will include the following ADA participant categories:

a) Category 2: Pre ADA negative – treatment-induced ADA positive
b) Category 4: Pre ADA positive – treatment unaffected ADA positive
c) Category 5: Pre ADA positive – treatment-boosted ADA positive

All categories will be presented on the same plot (visualized using different colors). Plots will be presented using a semi-logarithmic scale for the ADA titers (ADA negative samples will therefore be excluded from the plot).

A listing of anti-rozanolixizumab antibodies will include all derived results.

Serum complement (C3, C4) and cytokines and plasma complement (C3a, C5a)

Listing will be provided for serum complement (C3, C4) and cytokines and plasma complement sampling details (C3a, C5a).

5.5.2 Exploratory Analyses on the effect of rozanolixizumab on infection specific IgG

Observed values at baseline and at SFU and change from Baseline to SFU in IgG concentrations will be summarized descriptively for each treatment group for the following virus specific IgG concentrations

Tetanus specific IgG

Influenza A virus-specific IgG antibodies,

SARS Cov-2 antibodies for COVID-19 vaccinated and/or previously infected participants

For SARS-COV-2 antibodies, the summary table will present one row for vaccinated participants, a second row for previously infected participants, and a final row for those with both (if any). In addition to the summary table, the data for the above specific antibodies will be listed for all the collected timepoints.

5.5.3 Other Exploratory Analyses

- Post-dose infusion site pain visual analog scale (VAS) with IMP administration

The visual analog scale of injection site pain indicates the level of pain at the site of injection. It reaches from 0-100 mm with higher values for more severe pain and 0 for no pain.
Participants VAS (mm) will be summarized using descriptive statistics based on the SS by cohort and treatment group, and by method of infusion (Manual push/Safety syringe) and treatment group (rozanolixizumab, regardless of dose, or placebo).

- Pre-dose self-injection assessment questionnaire (SIAQ) for MP administration

There are 2 modules for the SIAQ: SIAQ PRE-Self-Injection and SIAQ POST-Self-Injection.

The SIAQ PRE-Self-Injection will be completed pre-dose by participants in the MP cohorts only.

It consists of 7 items each with a scale of 1 to 5. There are three individual domains (feelings about injections [FL, 3 items], self-confidence [CO, 3 items] and satisfaction with current mode of administration [SA, 1 item]). Each domain score will be calculated as the average of the individual transformed item scores. The item scores will be transformed using the following rule:

$$\text{Transformed Item Score} = ((\text{raw item score})-1)\times 2.5$$

In the case of missing values, a domain score will be calculated only if 50% or more of the items within the domain are completed.

The domain scores range from 0 to 10, higher scores indicate more confidence, higher satisfaction and less concerns with self-injections.

Participants pre-dose SIAQ domain scores will be summarized using descriptive statistics based on the SS by cohort and treatment group, and by treatment group only (rozanolixizumab, regardless of dose, or placebo).

- Post-dose self-injection assessment questionnaire (SIAQ) for MP administration

The SIAQ POST-Self-Injection will be completed 30 minutes to 1 hour post-dose by participants in the MP cohorts only.

It consists of 21 items on 6 individual domains (FL [3 items], self-image [IM, 1 item], CO [3 items], injection-site reactions [RE, 2 items], ease of use [EU, 5 items] and satisfaction with self-injection [SA, 7 items]). The items of the individual domain EU have a score range of 1 to 6, the items of the other individual domains have a score range of 1 to 5. Each domain score will be calculated as the average of the individual transformed item scores.

The item scores for the EU domain will be transformed using the following rule:

$$\text{Transformed Item Score} = ((\text{raw item score})-1)\times 2$$

The item scores for the other domains will be transformed using the following rule:

$$\text{Transformed Item Score} = ((\text{raw item score})-1)\times 2.5$$

In the case of missing values, a domain score will be calculated only if 50% or more of the items within the domain are completed.

The domain scores range from 0 to 10, higher scores indicate more confidence, higher satisfaction and less concerns with self-injections.

Participants post-dose SIAQ domain scores will be summarized using descriptive statistics based on the SS by cohort and treatment group, and by treatment group only (rozanolixizumab, regardless of dose, or placebo).

- Post-dose injection site reaction questionnaire (ISRQ) for syringe driver administration

The ISRQ will be completed 30 minutes to 1 hour post-dose by participants (syringe driver cohorts only).

The ISRQ consists of the items from the individual domain RE of the SIAQ POST-Self-Injection. The ISRQ score will be calculated as the average of the individual transformed item scores. The item scores will be transformed using the following rule:

$$\text{Transformed Item Score} = ((\text{raw item score})-1)\times 2.5$$

In the case of missing values, the ISQR score will be calculated only if 50% or more of the items are completed.

The ISQR score ranges from 0 to 10, higher score indicates less concerns with the injections.

Participants post-dose ISRQ score will be summarized using descriptive statistics based on the SS by cohort and treatment group, and by treatment group only (rozanolixizumab or placebo).

5.6 Safety Analyses

All safety analyses will be performed using the SS.

5.6.1 Extent of Exposure

All IMP administration details (including date/time of administration and volume administered) will be listed by treatment group and participant. The listing will include the start and stop time of the drug administration, the duration (derived) and details regarding any interruptions/ discontinuations including the reasons, if applicable.

Since the IMP administration consists of a [redacted] dose, duration of exposure will not be calculated.

5.6.2 Adverse Events

See Section 5.3 for a description of the analysis and reporting of adverse events.

5.6.3 Additional Safety Assessments

5.6.3.1 Clinical laboratory evaluations

Laboratory data (hematology, clinical chemistry, and urinalysis) and changes from Baseline (if applicable) for numeric variables will be listed by cohort, treatment group and time point. Only abnormal laboratory values will be listed. In case of any abnormal value, all values for the respective subject on this laboratory parameter will be listed.

Any laboratory measurements that are BLQ or above the limit of quantification (ALQ) will be handled as described in Section 6.1.5.1. Values outside the reference range for numeric variables will be flagged in the listings and in addition, will be listed separately for each lab category (hematology, chemistry and urinalysis). The reference ranges will also be reported in the listings.

Laboratory measurements satisfying the marked abnormality criteria (see Section 6.1.9.1) will be flagged.

Screening tests (as specified in Appendix 2 of the protocol) will be listed in a separate listing.

5.6.3.1.1 Laboratory values over time

Laboratory variables are grouped according to the laboratory function panel (see Appendix 2 of the protocol). Observed laboratory variables and changes from Baseline will be summarized by descriptive statistics at each time point by cohort, treatment group and method of administration based on SS. In addition, TEMAs for hematology and for clinical chemistry abnormalities will be summarized by treatment group and visit.

5.6.3.1.2 Individual Participant Changes of Laboratory Values

Laboratory variables will be categorized as normal, high or low, if applicable, based on the reference range supplied by the analytical laboratory. The change in category from Baseline will be presented in shift tables at all post-Baseline time points per cohort, treatment group and method of administration (refer section 5.1.1.3).

5.6.3.1.3 Potential Drug-Induced Liver Injury

Data from subjects with any of the laboratory results meeting the criteria for potential drug-induced liver injury (PDILI) (below) will be summarized by treatment group and visit.

PDILI Criteria:

- Alanine aminotransferase (ALT) or Aspartate aminotransferase (AST) ≥5x Upper limit of normal (ULN)

- ALT or AST increase ≥3x ULN and Total bilirubin ≥2x ULN

- (ALT or AST increase ≥3x ULN) and Total bilirubin ≥2x ULN and ALP <2 x ULN

- (ALT or AST ≥3x ULN) and (eCRF question for "Is the subject exhibiting we symptoms of hypersensitivity" = Yes or eCRF question for "Is the subject exhibiting symptoms of. Hepatitis" = Yes at the same date +/-2 days).

- (ALT or AST) ≥3xULN (and ≥2x Baseline) and <5xULN and Total bilirubin <2xULN and (eCRF question for "Is the subject exhibiting symptoms of hypersensitivity" = No and eCRF question for "Is the subject exhibiting symptoms of Hepatitis" = No at the same date +/-2 days)

- (ALT or AST) ≥5xULN (and ≥2x Baseline) and Total bilirubin <2xULN (eCRF question for "Is the subject exhibiting symptoms of hypersensitivity" = No and eCRF question for "Is the subject exhibiting symptoms of Hepatitis" = No at the same date +/-2 days)

A listing will also be created only visits for which at least one of the above criteria was fulfilled for a given participant and will display all results obtained at that visit for the specified parameters.

5.6.3.2 Vital Signs

The following vital signs measurements will be obtained with the participant resting in a supine position after 5 minutes rest:

- Pulse rate
- Systolic and diastolic blood pressure (BP)
- Temperature (tympanic)
- Respiratory rate

A by-participant listing of all vital sign measurements and change from Baseline will be presented by cohort and timepoint. The listing will include a flag for measurements identified as treatment-emergent markedly abnormal (TEMA) as calculated by the criteria outlined in Section 6.1.9.2.

5.6.3.2.1 Vital Sign Values Over Time

Descriptive statistics will be reported for all vital sign measurements. Measured values and changes from Baseline will be summarized by vital signs variables and timepoint for each cohort, treatment group and method of administration (refer section 5.1.1.3).

5.6.3.2.2 Individual Participant Changes of Vital Sign Values

The number and percentage of participants with TEMA vital sign values will be summarized by cohort, treatment group and method of administration(refer section 5.1.1.3) at each timepoint.

5.6.3.3 Electrocardiograms (ECGs)

All ECG recordings should be taken before any blood sampling (except at the end of infusion) and with the study participant resting in the supine position for at least 5 minutes before the recording.

The following ECG parameters will be reported:

- Heart rate
- PR interval
- QRS interval
- QT interval
- QT corrected for heart rate using Fridericia's formula (QTcF)

The individual measurements will be reported in the by-participant listings. The listing will also include the observed results, change from Baseline at each timepoint, and will be presented by cohort, treatment group, method of administration (refer section 5.1.1.3) and timepoint.

A listing of ECG findings, for participants with abnormal (whether or not clinically significant) results will be presented by cohort, treatment group, method of administration and time point.

ECG abnormality criteria can be found in Section 6.1.9.3.

5.6.3.3.1 Electrocardiogram Values Over Time

Measured values and changes from Baseline values will be summarized by cohort, treatment group (refer section 5.1.1.3) at each timepoint and by ECG variable. ECG TEMAs will be summarized by treatment group and visit.

5.6.3.3.2 Individual Participant Changes of Electrocardiograms Values

The following cut-points in QTcF (raw data and change from Baseline) data will be summarized categorically (number and percentage of participants) by cohort, treatment group (refer section 5.1.1.3) at each timepoint.

For raw data:

- <450msec
- ≥450 to <480msec
- ≥480 to <500msec
- ≥500msec

Absolute change from Baseline in QTcF:

- <30msec
- ≥30 to <60msec
- ≥60msec

5.6.3.4 Other safety endpoint(s)

Physical examination and body weight

Participants with abnormalities in the physical examination will be listed including details of the abnormality.

Photographs of Injection Site:

Details of whether photographs were taken, prior to start and 30 minutes after the end of the IMP administration, and the date if so, will be listed for each subject and study visit. Any additional photograph taken upon occurrence of any injection site reaction will also be listed.

Local tolerability of SC infusion

Assessment of local tolerability of SC infusion (by the investigator or designee) will be completed post-dose, at the end of infusion, and 4, 6, 8, 12, 24, 36, 48, 72, and 96 hours after the start of infusion. Summary and listings will be provided for the tolerability reaction details.

5.7 Other Analyses

No other analyses (including genomics) have been planned for this study.

5.8 Subgroup analyses

Not applicable, no subgroup analyses are planned for this study

5.9 Interim Analyses

No formal interim analyses are planned for this study.

5.10 Safety Monitoring Committee

As per the protocol defined cohort description, two sentinel study participants (1 active + 1 placebo) will be incorporated into Cohort 1 and a SMC will convene to evaluate all available safety and tolerability data following completion of the 72-hour evaluation period and prior to dosing of the remaining participants in Cohort 1.

An Operational Plan will be agreed between ICON and UCB to detail the timelines, data flow and review processes leading up to, and on the critical path for each SMC. The analysis of these safety data are outside the scope of this analysis plan.

6 SUPPORTING DOCUMENTATION

6.1 Appendix 1 Non-key analysis specifications

6.1.1 Baseline characteristics and demographics

A by-participant listing of demographics will be presented by cohort and treatment group (refer section 5.1.1.3) based on the ES. This will include the year of birth, age (in years), sex, race, ethnicity, height (in cm), weight (in kg) and body mass index (BMI). The height will be obtained only at screening. Body mass index in kg/m^2 is calculated based on the height (in m) and the weight (in kg) using the following formula:

$$\text{BMI } (kg/m^2) = \text{weight (kg)}/[\text{height (m)}]^2$$

The BMI will be reported to 1 decimal place.

All demographic characteristics (with the exception of year of birth) will be summarized by cohort and treatment group based on the SS. The summary of age will include descriptive statistics and categorical summaries, the latter based on requirements for EudraCT and clinicaltrials.gov reporting. For the EudraCT reporting, the categories will include:

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

For clinicaltrials.gov reporting, the categories will include:

- ≤18 years
- 19 to <65 years
- ≥65 years

Other Baseline characteristics

Lifestyle information (alcohol and illicit drugs) will be listed by cohort and treatment group (refer section 5.1.1.3) for the SS.

Childbearing Potential and Birth Control will be listed for the SS.

6.1.2 Protocol deviations

Important protocol deviations will be identified and classified by the deviation types in the IPD document.

A listing of all IPDs identified at the DEM and deviations related to COVID-19 will be presented based on the RS, and will include the deviation type and description. The number and percentage of participants in the RS with IPDs will be summarized by cohort and treatment group (refer section 5.1.1.3). The denominator for the percentages will be the number of participants in the RS. In addition, deviations related to COVID-19 will also be summarized.

The following information from the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing polymerase chain reaction (PCR) CRF form will be displayed in a separate listing: status of PCR test performed, date of sample, test result, impacted visit and date of visit, the impact category, relationship with COVID-19 and the narrative of event. The number and percentage of the impact categories will be summarized by cohort, treatment group and visit for the RS.

6.1.3 Medical history

Medical history will be listed and summarized (in an incidence table) for the SS by cohort, treatment group (refer section 5.1.1.3) and MedDRA SOC and PT.

Procedure history will be listed separately by cohort treatment group and the procedure reported term for the SS.

6.1.4 Prior/concomitant/follow-up medications

Prior and concomitant medications will be listed and summarized (in an incidence table) for the SS by cohort and treatment group (refer section 5.1.1.3), by WHODD Anatomical Main Group (Level 1 term text), Pharmacological Subgroup (Level 3 term text) and PT. The reported term will be included in the listing. Separate tabulations will be presented for prior medications and concomitant medications. Prior medications which are started prior to medication and continued after the treatment will also be classified as concomitant and will be included in both summaries.

Any prohibited concomitant medications (as defined in protocol section 6.5.2) will be identified via a medical review and flagged in this listing.

Past medications are defined as any medications that started prior to the first administration of study drug and stopped prior to dosing.

Concomitant medications includes any medication that has been taken at least once on or after the date of first administration of study drug (also referred to as **new onset of concomitant**

medications). Permitted concomitant medications are limited to those listed in section 6.5.1 of the protocol.

Prior and Concomitant medications (also referred to as **Baseline medications)** will include any medications that started prior to dosing and continued after (classified as prior and concomitant medications).

Two summary tables will be produced; a table summarizing all medications that started prior to the first administration of study drug which will include all "past medications" and all "prior & concomitant medications", and a table summarizing all concomitant medications which will include all "concomitant medications" and all "prior & concomitant medications". In addition a listing will be produced. Any medications with missing dates and/or times will be handled as described in Section 6.1.5.3 in order to classify them as prior or concomitant.

6.1.5 Data derivation rules

6.1.5.1 Laboratory data

Safety laboratory measurements that are BLQ will be imputed with half of the LLOQ for the purpose of calculating change from Baseline and for the summaries and figures. Measurements ALQ, if applicable, will be imputed to the upper quantification limit.

6.1.5.2 Pharmacokinetic concentration data

Concentrations that are BLQ will be imputed with half of the LLOQ for the purpose of calculating the geometric mean and its 95% CI, the geometric CV, the arithmetic mean and SD for summaries and figures. For this purpose missing values should be excluded. Descriptive statistics of concentrations will be calculated if at least two-third of the individual data points are quantifiable (≥LLOQ).

For all individual PK concentration plots any values that are BLQ will be imputed with half of the LLOQ, with the exception of pre-dose BLQ values (linear scale only) which will be imputed as zero.

6.1.5.3 Dates and times

Partially or completely missing dates may be imputed for the following reasons:

- Classification of AEs as treatment-emergent
- Classification of medications as past, prior or concomitant
- Duration of AEs

Imputed dates will not be shown in the listings; all dates will be displayed as reported in the database.

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

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

• If only day is missing, and month-year is:

  - the same as the month-year of the IMP administration then assign the day of IMP administration. If the imputed start date is after the specified end date, then assign first day of the month, or the day of screening date if this is later (if the latter imputation results in an end date that is earlier than the start date, then assign first day of the month);
  - not the same as the month-year of the first dose of IMP then assign the first day of the month.

If AE occurred on the same day as treatment start date, but with missing time, time will be imputed as the same time as treatment start time; If AE occurred prior or after treatment start date but with missing time, time will be imputed as 00:00h. If the start time of medication is missing, this will be imputed as 00:00h.

The following rules will be applied for partial stop dates:

- If only the month and year are specified, then use the last day of the month;
- If only the year is specified, then use December 31 of the known year;
- If the stop date is completely unknown, then use discharge date or data cut-off date.

Note: Discharge date refers to the date of the end of study visit for completed study participants or the date of discontinuation for study 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 study 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.

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

Missing or partially missing dates and/or times will be imputed as described in Table 6-1 for the calculation of duration of each AE. Adverse event duration is computed in and reported in day and time format: xx d hh:mm.

Table 6-1: Calculation rules for duration of AEs

Data Availability	Onset Date/ Time	Outcome Date/ Time	Calculation Rules
Complete data	D1/T1	D2/T2	Duration = [(D2 – D1)*24 + (T2 – T1)]/24 days
End time missing	D1/T1	D2/--	End time is substituted by time 23:59h (=23.98 in decimal format). Duration = <[(D2 – D1)*24 + (23.98 – T1)]/24 days
Start time missing	D1/--	D2/T2	Onset time is substituted by 00:00h. Duration = <[(D2 – D1)*24 + T2]/24 days. In case of an AE starting on the study drug intake day but with missing time, the time imputed is the dosing time and this time should be used for the duration calculation. For AE starting on a different days then study drug intake, then take 00:00.
Start and end time missing	D1/--	D2/--	Duration = < (D2 – D1) + 1 days
Start day and time missing	--/--	D2/T2	Duration = < [(D2 – D0)*24 + (T2 – T0)] / 24 days For a participant in the SS, D0 and T0 are the date and time of administration of IMP and for screen failures, D0 = the screening visit date and T0 = 0. If the 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 start date that is after the end date, then use January 01)".

Data Availability	Onset Date/ Time	Outcome Date/ Time	Calculation Rules
End day and time missing	D1/T1	--/--	For ongoing AE duration = > Discharge day – D1 (days) For resolved AE duration = < Discharge day – D1 (days) where discharge refers to the date of the Safety Follow-up visit or date of discontinuation. For any AEs with known start date/time after the date of discontinuation, the date of last contact will be used as the discharge day.
Start and end date missing	--/--	--/--	For ongoing AE duration = > Discharge day – D0 (days) For resolved AE duration = < Discharge day – D0 (days) where discharge refers to the date of the Safety Follow-up visit or date of discontinuation. For a participant in the SS, D0 is the date of administration of IMP and for screen failures, D0 =the screening visit date.

6.1.5.4 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:

- For repeated measurements obtained prior to dosing the latest value (which may be scheduled or unscheduled) will be used in the calculation of the descriptive statistics.
- For repeated measurements obtained at the designated Baseline visit, the latest values (which may be scheduled or unscheduled) will be defined as the Baseline provided that the measurement occurred prior to dosing.

6.1.6 AEs of Special Interest

An AE of special interest (AESI) is any AE that a regulatory authority has mandated be reported on an expedited basis, regardless of the seriousness, expectedness, or relatedness of the AE to the administration of a UCB product/compound. For rozanolixizumab, the following events require immediate reporting (within 24 hours regardless of seriousness) to UCB:

- Potential Hy's Law, defined as ≥3× upper limit of normal (ULN) alanine aminotransferase (ALT) or aspartate aminotransferase (AST) with coexisting ≥2×ULN total bilirubin in the absence of ≥2×ULN alkaline phosphatase (ALP), with no alternative explanation for the biochemical abnormality, must ALWAYS be reported to UCB as an AE of special interest (ie, without waiting for any additional etiologic investigations to have been concluded). Follow-up information should then be reported if an alternative etiology is identified during investigation and monitoring of the participant.

6.1.7 AEs of Special Monitoring

In addition, **AEs of special monitoring** have been identified.

These include:

- Severe headache

  Participants suffering from severe headache are requested to complete the headache questionnaire daily until the headache has been resolved. The results of this questionnaire will be listed.

  For participants with severe headache a neurological assessment may be performed at the investigators discretion. In addition a lumbar puncture for CSF collection and a CT scan may be performed. The results of these additional assessments will be listed as well.

- Severe gastrointestinal disturbances (i.e. abdominal pain, diarrhea or vomiting)

  Study participants who experience moderate or severe diarrhea will have a stool sample collected and analysed. The results of the stool sampling will be listed.

- Opportunistic infection

The number and percentage of participants who experience AEs of special monitoring and who experience AEs of special interest will be summarized by cohort, treatment group, and method of administration, SOC and PT based on the SS. The A listing will be presented by cohort and treatment group for all AEs of special interest/monitoring. Additionally symptoms and frequency of severe headaches will be listed.

6.1.8 AEs of Focus

The following AEs are defined in the Rozanolixizumab program as AEs of focus (please see Appendix 3 for more details)

− Headaches
− Gastrointestinal Disturbances
− Hypersensitivity Reactions
− Anaphylactic Reactions
− Injection Site Reactions
− Infusion Reactions
− Infections
− Opportunistic Infections
− Reductions in Albumin and Plasma Proteins

− Effects on the Kidney

− Drug Related Hepatic Disorders

− Effect on lipids

AEOFs will be summarized by treatment group to tabulate the following:

• Incidence of each AEOFs by SOC, High Level Group Term (HLGT), HLT and PT

• Incidence of each Serious AEOFs by SOC, High Level Group Term (HLGT), HLT and PT

• Incidence of each AEOFs by relationship, SOC, HLGT, HLT and PT

• Incidence of each AEOFs by maximum intensity, SOC, HLGT, HLT and PT

6.1.9 Abnormality Criteria for Laboratory, Vital Sign and Electrocardiogram Parameters

6.1.9.1 Laboratory Assessments Marked Abnormality Criteria

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 or graphical data summaries.

6.1.9.1.1 Hematology

PARAMETER	*UNIT (conventional)*	*UNIT (standard)*	*MARKED ABNORMALITY CRITERIA*
Hemoglobin	g/dL	g/L	<8.0 g/dL; <80 g/L
WBC (Leukocytes)[1]	10^9/L	10^9/L	Low: <2.0 x 10^9/L
			High: >30 x 10^9/L
Lymphocytes Absolute	10^9/L	10^9/L	Low: <0.5 x 10^9/L
			High: >20 x 10^9/L
Neutrophils Absolute	10^9/L	10^9/L	<1.0 x 10^9/L
Platelets[2]	10^9/L	10^9/L	<50.0 x 10^9/L

[1]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 RLZ, 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 10^9/L is applied to flag leukocytosis (George 2012).

[2]For blinded ITP protocols, Platelets will not be assessed for TEMA because this parameter will be blinded and is expected to be abnormally low due to the participant population and entry criteria.

6.1.9.1.2 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
Estimate glomerular filtrate rate (eGFR)[1]	mL/min/1.73 m	mL/min/1.73 m	eGFR <29 mL/min/1.73 m
C reactive protein (CRP)[2]	mg/L	mg/L	>10mg/L
Calcium	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
Immunoglobulin G[3]	(g/L)	(g/L)	≤1 g/L
Potassium	mmol/L	mmol/L	Low: <2.5 mmol/L
			High: >6.0 mmol/L
Sodium	mmol/L	mmol/L	Low: <125 mmol/L
			High: >155 mmol/L
Glucose[4]	mg/dL	mmol/L	Low: <40 mg/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-glutamyltransferase; L = liter; mg = milligram; mmol = millimoles; µg = microgram; U = unit; ULN = upper limit of normal

Note: Marked abnormality criteria are defined by Grade 3 or higher events according to the CTCAE, Version 5.0 unless otherwise noted.

[1]eGFR is calculated using the Chronic Kidney Disease Epidemiology Collaboration or CKD-EPI formula (https://qxmd.com/calculate/calculator_251/egfr-using-ckd-epi) which is eGFR = 141 * min(Scr/κ,1)$^{\alpha}$ * max(Scr/κ, 1)$^{-1.209}$ * 0.993^{Age} * 1.018 [if female] * 1.159 [if black]; where Scr is serum creatinine (mg/dL), κ is

0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1. For derivation from values in standard units (umol/L) the κ values are 61.88 for females and 79.56 for males.s

[2]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.

[3]Immunoglobulin G criterion based on immunodeficiency literature and noted in RLZ study protocols.

[4]Glucose high criterion defined by Grade 3 and higher events according to CTCAE, Version 4.03, June 14, 2010.

6.1.9.2 Vital signs

Abnormality criteria to be applied in the assessment of vital signs parameter values are given below.

PARAMETER	*ABNORMALITY CRITERIA*
Pulse Rate (beats/minute)	≤50 and a decrease from Baseline of ≥15 ≥120 and an increase from Baseline of ≥15
Systolic Blood Pressure (mmHg)	≤ 90 and a decrease from Baseline of ≥20 ≥ 180 and an increase from Baseline of ≥20
Diastolic Blood Pressure (mmHg)	≤50 and a decrease from Baseline of ≥15 ≥105 and an increase from Baseline of ≥ 15
Temperature	>101 ^{0}F (38.3 ^{0}C)
Body Weight	≥ 10% decrease from Baseline ≥ 10% increase from Baseline

6.1.9.3 Electrocardiogram (ECG)

Abnormality criteria to be applied in the assessment of ECG parameter values are given below:

Parameter	Abnormality Criteria
QT interval (ms)	≥500ms
	≥60ms increase from Baseline
QTc(F) (ms)	≥500ms
	≥60ms increase from Baseline
PR interval (ms)	Treatment-emergent value >200ms
QRS interval (ms)	Treatment-emergent value >100ms
Heart rate (bpm)	<50bpm
	>120bpm

Abbreviations: bpm = beats per minute; ms = milliseconds; QTc(F) = Fridericia corrected QT interval;
Note: Treatment-emergent is defined as meeting the criteria at any post-Baseline visit after the first infusion of study medication and within 56-days of the last infusion and not meeting the same criteria during Baseline

6.1.10 Compliance

Designated site personnel will ensure treatment compliance by overseeing SC infusion of the IMP by the participant. Drug accountability must be recorded on the Drug Accountability form. Any incomplete administration of IMP will require documentation of how much was infused (including start and stop times).

As a measure of compliance the percentage of the planned dose administered will be calculated based on the planned and delivered infusion volume:

Percentage of planned dose administered (%) = [100*(actual volume/planned volume)]

The actual dose administered will be calculated as:

Actual dose (mg) = (planned dose* (percentage of planned dose administered/100)).

The actual volume delivered, percentage of planned dose administered, actual dose (mg), duration of infusion (minutes) will be summarized descriptively. In addition the number of participants with infusion temporarily stopped and the number of participants with infusion permanently discontinued will be summarized.

A listing on compliance data will be prepared.

6.2 Appendix 2: Changes to Protocol-Planned Analyses

As per protocol "All safety variables will be analyzed by descriptive methods and presented by treatment (rozanolixizumab or placebo), method (MP or syringe driver), body weight, and dose level." However, the analysis were planned by cohort and treatment group as per the SAP section 5.1.1.3. All other analysis were planned as per the protocol.

6.3 Appendix 3: Adverse Events (AEs) of Focus for the Rozanolixizumab Program

The purpose of this document is to detail the approach to identifying TEAEs meeting criteria for AEs of focus (AEOF) for the Rozanolixizumab (also called Rozimab) program.

The document is organized by MedDRA version. At the time of writing this document, MedDRA version 22.0 was planned to be used for all indications under investigation (MG, ITP, CIDP, HV). As there is no change between 22.0 and 22.1 and 23.0 and 23.1 and 24.0 regarding terms used in below selection criteria, all below specified algorithms apply to these MedDRA versions. If future studies are planned which use a different (more recent) version of MedDRA, this document will be updated.

MedDRA SMQ file 24.0:

SMQ_spreadsheet_
24_0_English.xlsx

Following Events are Adverse Event of focus For Rozimab for all indications:

No	Event (also included in Title of TFL output)	Selection criteria	Purpose CSR/ SSD/ IB
1	Headache (Note: also included in AESM if severe)	TEAE with HLGT='Headaches'	CSR/ SSD/ IB
2	Gastrointestinal disturbances (Note: also included in AESM if severe)	TEAE with HLT='Gastrointestinal and abdominal pains (excl oral and throat)' or HLT='Gastrointestinal signs and symptoms NEC' or HLT='Nausea and vomiting symptoms' or HLT='Diarrhoea (excl infective)' or HLT='Gastritis (excl infective)'	CSR/ SSD/ IB
3	Hypersensitivity reactions	SMQ='Hypersensitivity'	CSR/ SSD/ IB
4	Anaphylactic reactions	SMQ='Anaphylactic reaction' and TEAEs that either emerged on the **same day** as when a study medication injection reaction was received, or that emerged **one day after** a study medication injection was received, and which fulfill any of the following 3 criteria should be included in the summary table: 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. 2. If a subject reports any TEAE which codes to a PT included in Category B **AND** reports any TEAE which codes to a PT included in Category C, **and both TEAEs have the same start date**, then both events will be flagged as anaphylactic reactions. 3. If a subject reports any TEAE which codes to a PT included in Category D **AND** reports (either a TEAE which codes	CSR/ SSD/ IB

		to a PT included in Category B **OR** a TEAE which codes to a PT included in Category C), **and both TEAEs have the same start date**, then both events will be flagged as anaphylactic reactions.	
5	Injection site reactions	TEAE with HLT='Injection site reactions' or HLT='Infusion site reactions' or HLT='Administration site reactions NEC'	CSR/ SSD/ IB
6	Infusion Reactions	Infusion reaction marked on AE CRF page (based on the assessment by the Investigator)	CSR/ SSD/ IB
7	Infections	TEAE with SOC ="Infections and infestations" **Note:** 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)	Opportunistic infections (including tuberculosis) will be summarized in a stand-alone table using UCB-defined search criteria. Opportunistic infections are identified in two steps using the attached spreadsheet for MedDRA v24.0: OI_MedDRA24_0.xlsx Step 1: Refer to column B of the spreadsheet which identifies the Preferred Terms (PTs) to be classified as opportunistic infections using either a single 'x' or a double 'xx'. • TEAEs which code to a PT flagged with a single 'x' need to also be serious in order to be considered an opportunistic infection. • All TEAEs which code to a PT flagged with a double 'xx' are considered to be an opportunistic infection, regardless of seriousness. All serious TEAEs in the study database which code to a PT flagged with a single 'x' and all TEAEs in the study database which	CSR/ SSD/ IB

		code to a PT flagged with a double 'xx' will be summarized as an opportunistic infection in the stand-alone table. [CQ97NAM= 'Opportunistic Infection - Automatic'] Step 2: Refer to column C of the spreadsheet which identifies the PTs that need to be evaluated on a case-by-case basis by the study physician and safety physician in order to determine whether it is a true opportunistic infection or not. The process for physician review is as follows: 1. Study programming team creates a spreadsheet which lists all of the subjects with a TEAE present in the database which codes to a PT identified as case-by-case. [CQ98NAM= Opportunistic Infection - Manual Review Candidate] Information from the AE dataset to be included in the spreadsheet: Subject ID, AE verbatim term, System Organ Class (SOC), High Level Term (HLT), Lower Level Term (LLT), PT, AE start date, AE end date, seriousness, severity, relationship to study medication, action taken. Additionally, a column will be included where the study physician/safety physician can document their decision on the case. 2. Study physician/safety physician (SPs) reviews the cases in the spreadsheet separately and reconciles final decision, and indicates in the additional column which AEs are confirmed to be opportunistic infections via a single 'x'. 3. Study programming team incorporates these decisions into the AE dataset by merging the SPs decisions for individual subjects / PTs and flagging both the automatic and the confirmed opportunistic infections as such in the dataset.	

		[CQ99NAM= 'Opportunistic Infection – Adjudicated'] The SPs reviews the context of all of a subject's data (AEs and possibly other) and concludes individually. Indicators of relevant cases may be e.g. repetitive occurrences, conjunction of other events or findings considered relevant. All subjects with a case-by-case PT reported that has been confirmed by the SPs to be an OI will be summarized as such in the stand-alone table, along with all of the events identified in Step 1 of this process. [CQ99NAM= 'Opportunistic Infection – Adjudicated'] The timing and frequency of Step 2 should be outlined and agreed to by the study team at the beginning of the study. It is suggested that this process be executed multiple times throughout the course of the study, more frequently in the weeks leading up to database lock, and one final time immediately prior to database lock. Following the initial physician review of case-by-case events, subsequent reviews will be based on the cumulative set of case-by-case events present in the database at each time point of spreadsheet creation. Physician decisions from previous runs should be retained in each subsequent run. The final run of the spreadsheet, with all SP decisions on the full set of case-by-case events, will be archived at the conclusion of the study analysis prepared for agency submission.	
9	Reductions in albumin and plasma proteins	TEAEs with PT='Blood albumin decreased' or PT='Protein albumin ratio' or LLT='Plasma protein abnormal' or LLT='Proteins serum plasma low'	CSR/ SSD/ IB
10	Effects on the kidney	TEAEs in SMQ= 'Acute renal failure'	CSR/ SSD/ IB
11	Drug related hepatic disorders	TEAEs in	CSR/ SSD/ IB

		SMQ='Drug related hepatic disorders - comprehensive 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'	CSR/ SSD/IB

For each of above-mentioned AEs of focus following analysis will be done:

Analysis	Table shell
Incidence of AEOF xxx	AE_T_02
Incidence of AEOF xxx by Relationship	AE_T_04b
Incidence of serious AEOF xxx	AE_T_02
Incidence of AEOF xxx by Maximum Intensity	AE_T_03A

The following output will only be requested as needed and will not be produced routinely: Incidence of TEAEs by Outcome, Time to onset of AEOF, Duration of AEOF, Kaplan-Meier plots of time to the first AEOF, AEs occurring 24hrs prior to TEAE of headache and 24hrs after

The standard medical history table should be updated to include HLGT or otherwise a separate medical history table need to be created to show all medical histories with HLGT=Headaches

For all indications for SSD/IB and CSR delivery:
A general Lab and AE excel file will be created (basically ADAE and ADLB as excel but limited by variables that will be shown in the standard listing) and named as AEOF ADxx YYYYMMDD
For ITP indication for final CSR TFLs delivery:

1. A separate Laboratory excel file for platelets need to be created for subjects with a platelet decrease of $10x10^9$/L or more after last Study Medication compared to baseline value. Suggested name for excel "AEOF Subjects who have a Change in Platelets from Baseline <= $-10x10^9$/L after last Study Medication YYYYMMDD
   Following variables should be included in Lab Listing:
   - Patient ID,
   - Actual Treatment group
   - Baseline Study medication dose,
   - Duration of the treatment
   - Last Study medication dose
   - Last PLT at the last study visit
   - Period
   - Visit
   - Date and Time of Measurement
   - Baseline PLT
   - PLT at Visit
   - Change from Baseline
   - Time to platelet drop after last IMP datetime.
   - Flag for Change <= - $10x10^9$/L
2. A separate AE excel file for Haemorrhages (SMQ) starting after last IMP date (=occurring in observation period)
3. A separate AE excel file for Haematopoietic thrombocytopenia (SMQ) starting after last IMP date (=occurring in observation period)

7 REFERENCES

CPMP/ICH/135/95 Note for guidance on Good Clinical Practice (EMEA) Jul 2002.

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