STATISTICAL ANALYSIS PLAN

AMENDMENT 1

Study: TP0004

Product: Rozanolixizumab

AN OPEN-LABEL EXTENSION STUDY TO INVESTIGATE THE LONG-TERM SAFETY, TOLERABILITY, AND EFFICACY OF ROZANOLIXIZUMAB IN STUDY PARTICIPANTS WITH PERSISTENT OR CHRONIC PRIMARY IMMUNE THROMBOCYTOPENIA (ITP)

SAP/Amendment Number	Date
Final SAP	01 Nov 2021
Amendment 1	21 Oct 2022

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List of Abbreviations

ADAs	Antidrug antibodies
AEOF	Adverse Events of Focus
AESI	Adverse Events of Special Interest
AESM	Adverse Events of Special Monitoring
BLQ	Below the limit of quantification
BP	Blood pressure
CP	Confirmed positive
CSR	Clinical Study Report
CV	Coefficient of variation
DEM	Data Evaluation Meeting
DNA	Deoxyribonucleic acid
eCRF	Electronic Case Report Form
ECG	Electrocardiogram
EOS	End of Study
EQ-5D-5L	European Quality of Life-5 Dimension 5 Level Assessment
ES	Enrolled Set
EW	Early withdrawal
FDA	Food and Drug Administration
geoCV	Geometric coefficient of variation
geoMean	Geometric mean
hCG	Human Chorionic Gonadotropin
HLT	High level term

HRQoL	Health-related quality of life
ICH	International Council for Harmonisation
IDMC	Independent Data Monitoring Committee
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IMP	Investigational medicinal product
ITP	Primary immune thrombocytopenia
ITP-BAT	ITP-specific Bleeding Assessment Tool
ITP-PAQ	ITP-Patient Assessment Questionnaire
LLOQ	Lower limit of quantification
MAP	Managed Access Program
MCS	Mental Component Summary
MedDRA	Medical Dictionary for Regulatory Activities
n	Number of participants
NCP	Not confirmed positive
OLE	Open Label Extension
PCS	Physical Component Summary
PD	Pharmacodynamic
PGI-C	Patient Global Impression of Change
PGI-S	Patient Global Impression of Severity
PK	Pharmacokinetic
PK-PPS	Pharmacokinetic Per Protocol Set
PROs	Patient reported outcomes

PT	Preferred term
RNA	Ribonucleic acid
RZL	Rozanolixizumab
SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	Standard deviation
SFU	Safety Follow-up
SF-36 V2	Short form 36-item
SIAQ	Self-Injection Assessment Questionnaire
SOC	System organ class
SS	Safety Set
TEAE	Treatment-emergent adverse event
TEMA	Treatment-emergent markedly abnormal
TFLs	Tables, figures, and listings
TPO	Thrombopoietin
TPO-RAs	Thrombopoietin-receptor agonists
ULN	Upper limit of normal

1 INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to provide all information that is necessary to perform the statistical analyses of study TP0004. 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 upon, and assumes familiarity with, the following documents:

Protocol Amendment 4: 04 Mar 2022
DMC Charter: 26 Apr 2021

The dosing regimen in the Original Protocol and Protocol Amendment 1 requiring a [redacted] administration of IMP was modified with Protocol Amendment 2: the IMP administration was changed to [redacted] Protocol Amendment 2 was not submitted to any regulatory authorities prior to issuance of Protocol Amendment 3.
After Protocol Amendment 3 was approved by the regulatory authorities, Protocol Amendment 4 was issued for correcting errors and inconsistencies from Protocol Amendment 3. Further details can be found in this SAP. All data will be analyzed based on the visits identified per the Schedule of Activities in the protocol that participant was enrolled in at the time of the assessment.

At the time this SAP was written, the sponsor had decided to terminate the parent studies TP0003 and TP0006 and consequently decided to terminate the TP0004 study prematurely by 30 December 2022.

If a future protocol amendment necessitates a substantial change to the statistical analysis of the study data, this SAP may be amended accordingly. The content of this SAP is compatible with the International Council for Harmonization (ICH) E9 Guidelines.
UCB is the Sponsor and PAREXEL is the Contract Research Organization (CRO) for this study.

Note: The term Investigational Medical Product (IMP), study medication, and study drug are used interchangeably in this document.

2 PROTOCOL SUMMARY

2.1 Study objectives

2.1.1 Primary objective

To assess the long-term safety and tolerability of treatment with rozanolixizumab.

2.1.2 Secondary objectives

- To assess the long-term clinical efficacy of treatment with rozanolixizumab
- To assess the effect of rozanolixizumab on study participant perceived symptoms
- To assess the reduction in use of steroids and other concomitant ITP medications

2.1.3 Exploratory objectives

- To assess the effect of rozanolixizumab on patient-reported outcomes (PROs)
- To assess the clinical efficacy of rozanolixizumab in study participants with first exposure to rozanolixizumab

- To assess effect of rozanolixizumab on health-related quality of life (HRQoL) and broader disease impact
- To assess resource utilization
- To assess the experience with the subcutaneous (sc) self-administration
- To assess the PD effect of rozanolixizumab
- To evaluate the incidence and emergence of antidrug antibody (ADA) of rozanolixizumab
- To assess the pharmacokinetics (PK) of rozanolixizumab administered by sc infusion
- To evaluate clinical response following end of dosing
- To assess the influence of rozanolixizumab treatment on vaccination titers
- To assess the effect of rozanolixizumab on post-vaccination biomarker(s) in study participants who received the COVID-19 vaccine

2.2 Study endpoints

2.2.1 Primary endpoints

2.2.1.1 Primary safety endpoints

- Occurrence of treatment-emergent adverse events (TEAEs)
- Occurrence of TEAEs leading to permanent withdrawal of rozanolixizumab (i.e., study discontinuation)

2.2.1.2 Other safety endpoints

- Occurrence of treatment-emergent adverse events of special monitoring (AESM)
- Occurrence of serious TEAEs
- Occurrence of treatment-related TEAEs
- Vital sign change from Baseline (blood pressure [BP], body temperature, and pulse rate) at each scheduled assessment during Treatment and Safety Follow-Up (SFU) Periods
- 12-lead electrocardiogram (ECG) change from Baseline at each scheduled ECG assessment visit
- Laboratory change from Baseline (hematology, including coagulation parameters, clinical chemistry, and urinalysis) at each scheduled assessment during Treatment and SFU Periods
- Changes from Baseline in concentrations of total protein and albumin
- Changes from Baseline in serum (C3 and C4) and plasma (C3a and C5a) complement levels at each scheduled assessment during study (for study participants experiencing infusion or hypersensitivity reactions)

2.2.2 Secondary endpoints

2.2.2.1 Secondary efficacy endpoint

- Stable Clinically Meaningful Response, defined as Clinically Meaningful Response (ie, platelet count $\geq 50\times10^9$/L) without rescue therapy at ≥70% of the visits over the planned 52 week Treatment Period starting at Week 4

2.2.2.2 Other efficacy endpoints

- Stable Response defined as platelet count $\geq 30\times10^9$/L and absence of bleeding[b] without rescue therapy at ≥70% of the visits over the planned 52-week Treatment Period starting at Week 4
- Cumulative number of weeks with Clinically Meaningful Response over the 52-week Treatment Period
- Cumulative number of weeks with platelet counts $\geq 30x10^9$/L over the planned 52-week Treatment Period
- Duration of first Clinically Meaningful Response starting at Week 4
- Mean Change from Baseline in platelet count at each visit
- Use of rescue medication by visit
- ITP specific Bleeding Assessment Tool (ITP-BAT) bleeding events and severity by visit

2.2.2.3 Other secondary endpoints

- Change from Baseline to Week 53 for ITP-PAQ Symptoms domain score
- AUC of the oral steroid dose over time
- Change in dose and/or frequency of concomitant ITP medications (excluding corticosteroids) over time

2.2.3 Exploratory endpoints

2.2.3.1 Exploratory efficacy endpoints (First Exposure Participants only)

- In study participants with first exposure to rozanolixizumab: Durable Clinically Meaningful Platelet Response of $\geq 50x10^9$/L, for at least 4 out of 6 [redacted] visits during Weeks 13-25 (of the OLE)
- In study participants with first exposure to rozanolixizumab: Time to first Clinically Meaningful Platelet Response of $\geq 50x10^9$/L: time from starting treatment to achievement of first response of $\geq 50x10^9$/L

2.2.3.2 Pharmacodynamic endpoints

- ADA at each scheduled assessment
- Total serum IgG (absolute value) and change from Baseline (absolute value and percentage) in serum IgG and in serum IgG subclass concentration at each scheduled assessment
- Absolute value and change from Baseline (absolute value and percentage) in serum Ig concentrations (IgA, IgE, IgM) at each scheduled assessment

2.2.3.3 Pharmacokinetic endpoints

- Plasma concentrations of rozanolixizumab at each scheduled assessment

2.2.3.4 Other exploratory endpoints

- Change from Baseline in FATIGUE-PRO Physical Fatigue Score
- Change from Baseline in Patient Global Impression of Severity (PGI-S)
- Patient Global Impression of Change (PGI-C) at all available post-Baseline assessments
- Change from Baseline in ITP-Patient Assessment Questionnaire (ITP-PAQ) domain scores
- Change from Baseline in European Quality of Life (EuroQol)-5 dimension 5 Levels Assessment (EQ-5D-5L) item responses
- Change from Baseline in Short-Form 36-Item (SF-36) domain and composite scores
- Number and length of hospitalizations
- Number of infusion center admissions
- PRE-Self Injection Assessment Questionnaire (SIAQ) (Infusion version) domains scores before the first sc self-administration in participants that self-administer
- POST-SIAQ (Infusion version) domains scores at each available visit in participants that self-administer
- Platelet count by visit after end of dosing
- Time from end of rozanolixizumab dosing to loss of clinically relevant response
- Percent change from Baseline in vaccination titers against *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* in splenectomized study participants
- Change in post-vaccination biomarker(s) over time in study participants who received the COVID-19 vaccine

2.3 Study design and conduct

This is a Phase 3, multicenter, 59-week OLE study of rozanolixizumab in study participants with persistent or chronic primary ITP. Study participants from TP0003 and TP0006 who have completed the 24-week Treatment Period (irrespective of rescue therapy) and continue to meet the eligibility criteria will be offered enrollment into TP0004.

This study will assess whether continued dosing [redacted] with rozanolixizumab is safe and well tolerated. This study will also assess whether continued rozanolixizumab sc infusions [redacted] over a period of 52 weeks will maintain a durable Clinically Meaningful Platelet count of $\geq 50 \times 10^9$/L.

The rollover from TP0003 or TP0006 to TP0004 needs to be completed within 3 days after Week 25 (Visit 27) of the parent studies at the latest. In case of a late rollover, platelet counts will need to be remeasured.

On Day 1 (Baseline Visit), which corresponds to Week 25 of the parent studies, TP0003 or TP0006, all study participants will enter TP0004. The study participants assigned to rozanolixizumab during the parent study will receive rozanolixizumab treatment [redacted] at the

assigned dose level at the end of TP0003 or TP0006, if the platelet count was between $\geq 50\times10^9$/L and $\leq 150\times10^9$/L. If outside of this range, a higher or lower dose level than the final sc infusion in TP0003 or TP0006 is permitted according to Table 4-2 and Figure 4-1 (in the Protocol). Study participants previously randomized to placebo, will enter the study and begin rozanolixizumab treatment on the assigned (placebo) dose level received at the end of the parent studies; thereafter doses can be adjusted if platelets are outside the targeted range. Rozanolixizumab will be administered [redacted] as a sc infusion to maintain platelet count $\geq 50\times10^9$/L. Dose levels equivalent to [redacted] and [redacted] total dose (corresponding to an average [redacted] dose in a participant weighing 70kg) [redacted] can be utilized for maintenance treatment.

If treatment with rozanolixizumab does not lead to an increase in platelet counts $\geq 30\times10^9$/L, study participants can be treated with rescue therapy if deemed needed by the investigator. If platelet counts are $\geq 10\times10^9$/L to $<30\times10^9$/L or active bleeding, rescue therapy is recommended (e.g., commercially available medication, such as intravenous immunoglobulin (IVIg), high dose corticosteroids and pulse steroids, platelet transfusions, or any other medication listed in Section 6.4.3 in the Protocol). If platelet counts are $<10\times10^9$/L, rescue therapy is highly recommended as per Section 6.4.3.

An external Independent Data Monitoring Committee (IDMC) will be utilized to review the safety data at predefined intervals and ad hoc as needed, should any emerging safety concern arise during the study. Key safety data may be pooled at the discretion of the IDMC for protection of all study participants if warranted.

Based on feedback from the IDMC, [redacted] dosing was introduced in protocol amendment 2. Study participants being treated with the [redacted] dosing regimen were switched to the [redacted] dosing regimen once protocol amendment 3 was approved at the respective study site.

Additionally, the sponsor's Safety Signal Detection Team will perform aggregated safety data reviews at predefined intervals across the rozanolixizumab program.

Based on the number of study participants planned for the parent studies, up to a maximum of 180 study participants who complete TP0003 or TP0006 may be eligible to enroll in this OLE study.

2.4 Determination of sample size

No formal sample size calculation can be performed. All participants from the parent studies (TP0003 and TP0006) interested and eligible for the OLE will be included. It is expected that up to a maximum of 180 participants will be included.

Note: Due to the premature termination of the study, only 43 participants did enroll into the OLE study.

3 DATA ANALYSIS CONSIDERATIONS

3.1 General presentation of summaries and analyses

Statistical analysis and generation of tables, figures, participant data listings, and statistical output will be performed using SAS® Version 9.4 or higher (SAS Institute, Cary, NC, USA).

All tables, figures and listings will use Courier New font size 9.

Descriptive statistics will be displayed to provide an overview of the study results. For continuous variables, descriptive statistics will include number of participants with available measurements (n), mean, standard deviation (SD), median, minimum, and maximum.

For categorical variables, the number and percentage of participants in each category will be presented. Unless otherwise noted, the denominator for percentages will be based on the number of participants included in the respective analysis set. Participants with missing data can generally be accounted for using the following approaches:

- For summaries of demographics and Baseline characteristics: summarize percentages based on all participants in the analysis set and include a "Missing" category (corresponding to participants with missing data for the variable being summarized) as the last row in the list of categories being summarized.
- For summaries of efficacy and safety variables, unless otherwise specified: summarize percentages based only on those participants with observed data for the variable being summarized. As the denominator may be different from the number of participants in the analysis set being considered, the denominator should be displayed in the table. The general format for displaying this will be "n/Nsub (%)."

Unless otherwise noted, all percentages will be displayed to one decimal place. No percentage will be displayed for zero counts, and no decimal will be presented when the percentage is 100%.

Tables which contain no data as no subject have met the criteria will display "No participants have met the criteria."

For the purpose of the tabulations the lower and upper confidence limits for the percentages will be truncated at 0 and 100% respectively.

For PK concentrations, summary statistics will include geometric mean, geometric coefficient of variation (CV), 95% confidence intervals (CIs) for geometric mean, arithmetic mean, SD, median, minimum, and maximum. All summaries of PK variables will be based on the observed values. No imputation will be used.

Decimal places for descriptive statistics will always apply the following rules:

- "n" will be an integer
- Mean, SD, and median will use one additional decimal place compared to the original data
- CV [%] will be presented with one 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, for example, then only n=0 will be presented. However, if n<3, present the n, minimum and maximum only. If n=3, n, mean, median, minimum, and maximum will be presented only. The other descriptive statistics will be left blank.

Derived variables in general will display the mean, SD and median to 1 more decimal place than the variables used in the derivation. If the number of decimal places reported in the raw data is varied, then use either the maximum raw number of reported decimal places or 3, whichever is the lowest, as a guide for the descriptive statistics.

3.2 General study level definitions

3.2.1 Analysis time points

All data will be analyzed based on the visits identified per the Schedule of Activities in the protocol that participant was enrolled in at the time of the assessment.

Mapping to visit windows will not be applied. For Early Withdrawal visits refer to Section 3.2.3

3.2.1.1 Relative day

Relative day for an event will be derived with the date of the first sc infusion of study drug which will occur at Baseline (Day 1)

Relative days for an event or measurement occurring before the date of first sc infusion will be prefixed with '-' and are calculated as follows:

Relative Day = [(Event Date – Date of First Infusion)]

The relative day for an event or measurement occurring on or after the reference date to the date of the first infusion is calculated as follows:

Relative Day = [(Event Date - Date of First Infusion) + 1]

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

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

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 participant data listings.

3.2.2 Study periods

As detailed in the Schedule of Activities in the Protocol, the following study periods are defined for this trial:

- **Treatment Period:** Starts on the day of the first dose administration of study drug (Day 1) and ends after the Week 53 or Week 55 visit assessments (or at the EW Visit for study participants withdrawn from the study before the Week 53 or 55 visit), depending on the protocol in place at the time final assessments were performed.
- **Safety Follow-up Period (SFU):** Starts with last dose administered and ends 8 weeks after final dose administered.

A study participant is considered to have completed the study if he/she has completed both the Treatment and Safety Follow-up Periods of the study including the SFU Period.

A study participant will be said to have completed the SFU period if she/he had completed the last scheduled visit in the SFU period.

Study participants will have an EOS Visit performed 8 weeks after the final dose of IMP (unless they are enrolling in TP0009 at week 53 or 55), or upon discontinuation of the study.

3.2.3 Mapping of assessments performed at Early Withdrawal Visit

Early Withdrawal assessments will be assigned to the next scheduled site visit (following the last scheduled visit that the participant completed prior to EW). Only EW assessments will be performed on this mapped visit.

3.2.4 Definitions Regarding the Dosing Regimen

Based on feedback from the IDMC, [redacted] dosing was introduced in protocol amendment 2. Study participants being treated with the [redacted] dosing regimen were switched to the [redacted] dosing regimen once the protocol amendment 3 was approved at the respective study site.

For the purpose of this SAP, presentation "by Dosing Regimen" refers to the presentation of assessments based on whether the participant was receiving [redacted] or [redacted] dosing of rozanolixizumab at the time the assessment or event occurred.

As soon as Protocol Amendment 3 was approved at each site, the participants who started TP0004 on [redacted] dosing and did not yet complete the treatment period, were allowed to either transition to [redacted] dosing or discontinue treatment (in accordance to Protocol Amendment 3 and subsequent versions).

Summary tables and listings presented by timepoint will be separated by dosing regimen. Timepoint summaries will be split by whether the participant was receiving [redacted] or [redacted] dosing at the time of the assessment (ie, took place before or after being dosed under Protocol Amendment 3) as applicable. All [redacted] dosing assigned visits will be presented before [redacted] dosing assigned visits.

3.2.5 General Considerations for Exploratory Arm Participants

Based on the changes made in Protocol Amendment 2 and subsequent protocol versions of TP0004, the Exploratory Treatment portion of the study design has been removed. For participants who took part in the Exploratory Treatment Arm prior to the implementation of Protocol Amendment 3 (protocol amendment 2 was never implemented), only visits and assessments (scheduled and/or unscheduled) prior to the start of the Exploratory Treatment Arm (Visit 19, Week 25 of Protocol Amendment 1) will be included in the summaries and figures related to the analysis of the endpoints detailed in this SAP. All other visits and assessments (and corresponding data) collected after the start of the Exploratory Treatment Arm will be listed.

3.3 Definitions of Baseline values

As stated in the Protocol, the Baseline Visit in TP0004 will correspond to the Week 25 of the parent studies (TP0003/TP0006). Baseline in TP0004 will be defined as the last available pre-dose value prior to the first infusion of study drug in the TP0004 Treatment Period (i.e., Visit 1/BL) unless otherwise stated. For the purpose of this SAP, Visit 1/BL refers to the nomenclature used in the Schedule of Activities (Table 1-1) in the Protocol, which is the equivalent to Baseline or Week 1 Day 1 in the eCRF.

When applicable (as specified in Table 1-1 of the Protocol, and their corresponding SAP sections), data will be transferred from the Screening or Baseline Visit of TP0003/TP0006 for the following values:

- Demographics

- Baseline Disease History

Scheduled or unscheduled measurements can be used as the Baseline value. If an unscheduled measurement occurs after the planned baseline measurement time point but before dosing, then the unscheduled measurement will be used.

3.4 Protocol deviations

Important protocol deviations are deviations from the protocol which potentially could have a meaningful impact on study conduct or on the primary safety, key efficacy, or PK/PD outcomes (if applicable) for an individual 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 ongoing data cleaning process and data evaluation. All important deviations will be identified and documented prior to unblinding to confirm exclusion from analysis sets.

3.5 Analysis sets

3.5.1 Enrolled Set (ES)

All study participants who have signed the informed consent.

3.5.2 Safety Set (SS)

All study participants who received at least 1 dose of IMP (partial or full). Analysis of this set will be according to the treatment the participants actually received, and will be used for the efficacy, demographic, PK, and safety analyses.

3.5.3 Pharmacokinetic Per-Protocol Set (PK-PPS)

A subset of the Safety Set, consisting of those study participants who received at least 1 dose and had at least 1 valid PK measurement and no important protocol deviations affecting the PK variable, as confirmed during a pre-analysis review of the data prior to database lock.

3.6 Center pooling strategy

It is planned to recruit participants in North America, Europe, and Asia in this study, with possible extension to other regions and countries. The data from all sites will be pooled for analysis purposes using the following geographical regions: North America, Europe, Asia (excluding Japan), and Japan.

3.7 Coding dictionaries

Adverse events (AEs) will be coded using version 24.0 or later of the Medical Dictionary for Regulatory Activities (MedDRA®).

Medications will be coded according to version Mar2021 or later of the World Health Organization Drug Dictionary (WHODD). Medical procedures will not be coded.

3.8 Changes to protocol-defined analyses

(1) Added COVID-19 as an intercurrent event to all endpoints

(2) Change from Baseline will not be calculated for the following safety endpoints. Only raw data will be listed.

- Vital signs change from Baseline (blood pressure [BP], pulse rate, body temperature) at each scheduled assessment during Treatment and SFU Periods
- 12-lead echocardiogram (ECG) change from Baseline at each scheduled ECG visit
- Laboratory change from Baseline (hematology including coagulation parameters, clinical chemistry, and urinalysis) at each scheduled assessment during Treatment and SFU Periods
- Change from Baseline in concentrations of total protein and albumin
- Change from Baseline in serum complement levels (C3 and C4) and plasma complement levels (C3a and C5a) at each scheduled assessment during the study (for study participants experiencing infusion reactions or hypersensitivity reactions)
- Absolute values and change from Baseline (absolute values and percentage) in serum immunoglobulin concentrations (IgA, IgE, IgM) at each scheduled assessment

(3) No formal statistical analyses of efficacy endpoints will be conducted. Only the following secondary efficacy endpoint(s) will be summarized descriptively and listed:

- Stable Clinically Meaningful Response - platelet count ≥50x109/L without rescue therapy at ≥70% of the visits
- Change from Baseline to Week 53 including all intermediate timepoints for ITP-PAQ Symptoms domain score

(4) The following changes are made to endpoints

- Remove "including all intermediate endpoints" in "Change from Baseline to **Week 53 or 55** for ITP-PAQ Symptoms domain score" and added "Week 55"
- Add endpoint "Clinically Meaningful Response at each Visit"
- "AUC of the oral steroid dose over time" changed to "Percent Change from Baseline in Oral Steroid Dose Over Time" and changed from secondary to "other" endpoint
- "Change in dose and/or frequency of concomitant ITP medications (excluding corticosteroids) over time" Changed to "Percent Change from Baseline in Concomitant ITP Medications (excluding Corticosteroids) Over Time" and changed from secondary to "other" endpoint

(5) Subgroup analyses to the secondary efficacy analysis will not be performed

(6) Analysis for the PMDA on the Japanese subset of participants will not be performed

(7) Change from baseline will not be calculated for the following endpoints. Only item responses will be listed.

- Change from Baseline in European Quality of Life-5 Dimension 5 Levels (EQ-5D-5L) item responses
- Change from Baseline in Short form 36-item (SF-36) domain and composite scores
- Change from Baseline in the ITP-PAQ V1 domain Scores (except for Symptoms score)
- Change from Baseline in FATIGUE-PRO Physical Fatigue Score by visit

- Change from Baseline in Patient Global Impression of Severity (PGI-S)

(8) Percent change from Baseline will not be calculated for the following endpoint. Titers will be listed.

- Percent change from Baseline in vaccination titers against *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* in splenectomized study participants

(9) Definition of PK-PPS changed to "A subset of the Safety Set, consisting of those study participants who received at least 1 dose **and had at least 1 valid PK measurement and no important protocol deviations affecting the PK variable, as confirmed during a pre-analysis review of the data prior to database lock.**"

4 STATISTICAL/ANALYTICAL ISSUES

4.1 Handling of dropouts or missing data

4.1.1 Handling of missing data for the primary safety endpoints

The primary safety analysis is based on a "treatment policy" estimand to allow for the inclusion of study participants that receive rescue medication. Regardless of a participant's initial dosing regimen at the start of TP0004 ([redacted] or [redacted] dosing), missing safety values will not be imputed; all available data will be reported.

4.1.2 Handling missing data for the secondary endpoints

Study participants who have not met the threshold for Stable Clinically Meaningful Response will be imputed as non-responders for the analysis. Missing platelet data at any visit will be considered "worst case" and set to zero ("no response") for that specific visit. Missing data for the ITP PAQ instrument will not be imputed.

For the secondary efficacy analysis, participants with intercurrent events will be considered as non-responders unless otherwise stated.

Missing data strategy for PRO related endpoints will follow instructions indicated in each instrument.

4.1.3 Missing Data due to COVID-19

For the purpose of this SAP, study participants who have visits impacted by COVID-19 for any reason [e.g., confirmed coronavirus disease (COVID-19) infection (e.g., signs/symptoms such as fever, cough, shortness of breath), or known exposure sufficient to necessitate testing or self-imposed quarantine] will be imputed as non-responders for the analysis at the corresponding visit. Missing platelet count data due to COVID-19 will be considered worst case and set to zero ("no response") for that specific visit.

4.1.4 Dates and times

Partial and completely missing dates may be imputed for the following reasons:

- Classification of Adverse events (AEs) as treatment-emergent
- Classification of medications as prior or concomitant
- Duration of AEs.

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

The following rules will be applied for **partial start dates:**

- If only start month and year are specified and are not the same as month and year of first dosing, then use the 1st of the month.
- If only the month and year are specified and the month and year of first dosing is the same as the month and year of the start date, then use the date of first dosing. If this results in an imputed start date that is after the specified end date, then use the 1st of the start month, 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 the 1st of the month).
- If only the year is specified, and the year of dosing is not the same as the year of the start date then use 01 Jan of the year of the start date.
- If only the year is specified, and the year of dosing is the same as the year of the start date, then use the date of first dosing. If this results in an imputed start date that is after the specified end date, then use 01 Jan of the year of the start 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 01 Jan).
- If the start date is completely unknown, then use the date of first dosing. If this results in an imputed start date that is after the specified end date, then use 01 Jan 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 01 Jan).

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

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, do not impute the stop date, except for ITP medications where end date is missing and ongoing is ticked as "no", which will be imputed as "Past" medications.

Table 4–1: Calculation rules for duration of AEs

Data availability	Onset date	Outcome date	Calculation rules
Complete data	Analysis Start Date (D1)	Analysis End Date (D2)	Duration = (D2 – D1) + 1 day
Start date missing	--	D2	Duration ≤ (D2 – D0) + 1 day Note: D0 = imputed dose start date per partial stop dates.

Data availability	Onset date	Outcome date	Calculation rules
End date partially or completely missing	D1	--	**If end date is completely missing, then:** **For ongoing AE:** Duration ≥ (Discharge Day – D1) + 1 day OR Duration ≥ (Data cut-off day) – D1 + 1 day **For resolved AE:** Duration ≤ (Discharge Day – D1) + 1 day OR Duration ≤ (Data Cut-Off Day) – D1 day Note: Where discharge refers to the date when the participant rolls over to TP0009, or the date of the end of study visit for completed participants or the date of discontinuation for participants that were withdrawn. **If end date is partially missing**, then: Duration = (D3 – D1) + 1 day Note: D3 is the imputed end date using partial stop dates (see above). For any AEs with known start date, if the end date is missing, the date of last contact will be used as the discharge day. 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.

Data availability	Onset date	Outcome date	Calculation rules
Start and end date missing partially or completely missing	--	--	**For ongoing AE:** Duration ≥ (Discharge Day – D0) + 1 day OR Duration ≥ (Data cut-off day – D0) + 1 day **For resolved AE:** Duration ≤ (Discharge Day – D0) + 1 day OR Duration ≤ (Data Cut-Off Day – D0) + 1 day For a participant in the SS, D0 is the date of first administration of IMP, and for participants excluded from the SS, D0 is the date of signing the informed consent. Note: Discharge refers to the date of the end of study visit 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 day. 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.

4.2 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 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 (ie, Screening and/or Baseline)
- For repeated or unscheduled measurements obtained at the designated Baseline visit, the latest non-missing value (scheduled or unscheduled) will be defined as the Baseline record that occurred prior to the first dose of IMP
- For any scheduled measurement obtained at any time point after the first dose of IMP is missing, unscheduled measurements will not be used for any missing assessment.
- See Section 8.4 for the rules applied to ECG triplicate measurements.

4.3 Handling and definition of the Corticosteroid (CS) prednisone equivalent dose

For the purposes of further analysis and tabulations, all corticosteroid doses (including both prior and concomitant corticosteroids taken for any indication) will be converted to prednisone equivalent doses. The conversion table for systemic corticosteroids is presented in Table 4-2.

Systemic corticosteroids are those with a route of administration of oral, intravenous, or intramuscular. All others (including topical, ocular, nasal, subcutaneous, intraarticular, etc.) will be considered non-systemic steroids which will have a prednisone equivalent dose = 0mg/day.

Budenoside is considered non-systemic even if taken orally and will always be assigned a prednisone equivalent dose = 0mg/day.

The prednisone equivalent dose will be included in the listing.

For example, if the total daily dose of triamcinolone is 8mg, the equivalent total daily dose of prednisone will be 10mg. If a new corticosteroid is reported that is not in Table 4-2, the appropriate prednisone equivalent conversion will be determined and the prednisone equivalent dose will be included in a separate systemic corticosteroids concomitant medication listing.

If medications are available in ATC 2 code [redacted] which are not in table below, then the dose equivalent to 5mg/day Prednisone will be provided by the physician for this new system CS and the TFL footnote will be updated with this information for the newly identified CS

Table 4-2: Prednisone equivalent doses of systemic corticosteroids/steroids

Corticosteroids /Steroids	Dose equivalent to 5mg/day Prednisone
Cortisone	25
Hydrocortisone	20
Deflazacort	6.5
Prednisone	5
Prednisolone	5
Methylprednisolone	4
Triamcinolone	4
Dexamethasone	0.75
Betamethasone	0.6

Notes:

- All non-systemic corticosteroids (including topical, ocular, nasal, subcutaneous, intra articular, etc.) will be assigned a prednisone equivalent dose = 0 mg/day.
- [redacted] "CORTICOSTEROIDS FOR SYSTEMIC USE, [redacted]"

4.4 Data Monitoring

An external IDMC will be established to review the safety data at predefined intervals and ad hoc as needed should emerging safety concerns arise during the study.

Details of the IDMC composition, processes, and responsibilities will be documented in the IDMC charter. The IDMC will be the same as used for the parent studies TP0003 and TP0006, but data from each study will be presented separately. Key safety data may be pooled at the discretion of the IDMC for protection of all study participants if warranted. The IDMC will oversee the safety of the study by reviewing safety data at periodic data reviews. The IDMC will consist of members independent from UCB. Study enrollment will not be halted during planned IDMC review of the safety and efficacy data. The objectives and procedures for the IDMC will be detailed in the IDMC Charter.

After parent studies are completed, TP0004 will not have its own IDMC but will fall under the program-independent DMC (PiDMC) instead.

4.5 Multicenter studies

This is a multicenter study; however, individual center's results will not be presented.

4.6 Examination of subgroups

Subgroups will no longer be examined.

5 STUDY POPULATION CHARACTERISTICS

5.1 Subject disposition

The following outputs will be created.

Summaries:

- **Reasons for ineligibility** (as collected on the Eligibility Criteria CRF page) will be summarized using the ES for all study participants who failed to meet eligibility criteria for TP0004.
- **Disposition of Study Participants Enrolled** will be summarized using the ES for overall, by region and by site. In this summary, the site number, principal investigator name, first subject in date, last subject out date, will be captured by each analysis set (ES, SS, PK-PPS).
- **Disposition of Analysis Sets:** summary of disposition of study participants by analysis sets (ES, SS, PK-PPS) using the ES.
- **Disposition and Discontinuation Reasons**, using the ES will contain the number and percentage of study participants who:
  - Started study and started each study period (Treatment Period and SFU Period)
  - Completed the study / study period
  - Discontinued study / study period
    - Primary Reason for discontinuation (premature study termination as collected in the Study Termination CRF).

- **Discontinuation due to AEs**, using the ES to tabulate the total number of study participants who discontinued the study due to AEs and the categories: AE serious fatal, AE non-fatal and other (AE non-serious, fatal).
- **COVID-19 Disposition:** Disposition and discontinuation reasons using the ES will contain the number and percentage of study participants (overall and by dosing regimen) who started, completed and permanently discontinued Treatment Period / Safety Follow-Up Period overall and by pre-, during and post- COVID-19 pandemic based on the start, completed and discontinuation date relative to the pandemic cut-off date (20 March 2020 start date, no end date). The discontinuation reason in each period will also be summarized. Discontinuation due to COVID-19 pandemic will be listed as sub-category under "Other" reason.

5.2 Protocol deviations

Important Protocol deviations will be summarized using the ES to include:

Number and percentage of participants with:

a. No important protocol deviations

b. At least one protocol deviation in the following categories
   - Inclusion criteria
   - Exclusion criteria
   - Withdrawal criteria
   - Prohibited concomitant medication use
   - Incorrect treatment or dose
   - Treatment non-compliance
   - Procedural non-compliance

c. Number of Participants excluded from the PK-PPS (and all categories in item b above).

A by-study participant listing of important protocol deviations will be provided using the ES.

Note: The criteria for exclusion of study participants and/or study data from the PK-PPS will be defined in the Protocol Deviation Specification document.

6 DEMOGRAPHICS AND OTHER BASELINE CHARACTERISTICS

Unless otherwise specified, all summaries will be based on the ES.

6.1 Demographics

Demographic variables collected at Screening or Baseline Visit, or Week 25 (Visit 28) of TP0003 or TP0006, as applicable, will be summarized on the ES using descriptive statistics, by categories mentioned below.

Categories for continuous variables (including n, mean, SD, Median, Min and Max):

- Age (years) - at the time of study entry
- Weight (kg)
- Height (cm)
- BMI (kg/m^2) calculated as: $BMI = \frac{\text{Weight (kg)}}{(\text{Height (m)})^2}$

Categorical variables (using frequency counts and percentages):

- Age (18 - < 65, 65 - < 85, ≥ 85 years)
- Age (≤ 18, 19 - < 65, ≥ 65 years)
- BMI (< 25, 25 - < 30, ≥ 30 kg/m^2)

- Weight (< 50kg, 50kg - < 70 kg, 70 - < 100kg, ≥ 100kg)
- Gender (Male, Female)
- Race (American Indian or Alaska native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Other/Mixed)
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino)
- Region (North America, Europe, Asia [excluding Japan], Japan)
- Country
- Parent study Where Participant Originated From: TP0003 or TP0006
- First Time Exposed to RLZ (Rozanolixizumab) (Yes/No)

By-study participant listings of demographics will be provided.

Childbearing potential will be listed for the ES.

6.2 Other Baseline characteristics

6.2.1 Baseline disease characteristics

The following will be summarized using descriptive statistics at baseline of the parent study unless stated otherwise (using ES):

- Age at first ITP diagnosis (years)
- Time since first confirmed diagnosis of ITP (years) (as collected in the eCRF)
- Splenectomy (Yes/No)
- IgG level (g/L) for
  - Non-splenectomized participants
  - Splenectomized participants
- Platelet count ($x10^9$/L) (as collected in the eCRF)
- Degree of thrombocytopenia (platelet count < or ≥$15x10^9$/L) (using data collected in the eCRF)
- ITP Duration (persistent or chronic primary ITP at time of enrolment into parent study, as defined in Section)
- Total Number of Prior Unique ITP Medications (as collected in Parent study eCRF)
- Total Number of Prior ITP Medications (as collected in Parent study eCRF)
- Number of past ITP Medications (as collected in Parent study eCRF)(1, 2, and ≥3)
- Concomitant use of TPO-RAs (e.g., Eltrombopag and Avatrombopag) (Yes/No)

Notes:

- Persistent or chronic primary ITP as defined in Section 2.3
- Data will be summarized using data captured or derived from eCRF.

- The duration of ITP for chronic ITP participants will be computed in years and it will be calculated as follows:

  $\frac{\text{Date of Screening} - \text{Date of Diagnosis}}{365.25}$, where Date of Screening is from the parent study, and the date of diagnosis will be obtained from the ITP history eCRF page.

- The duration of ITP – for persistent ITP participants will be computed in months and it will be calculated as :

  $\frac{\text{Date of Screening} - \text{Date of Diagnosis}}{30.5}$, where Date of Screening is from the parent study, and the date of diagnosis will be obtained from the ITP history eCRF page.

- Age at diagnosis (years) will be calculated as: $\frac{\text{Date of diagnosis} - \text{Date of birth}}{365.25}$

- If the date of diagnosis is missing, the duration of disease and age at diagnosis will not be calculated. In the case of the start day being missing, the day will be imputed with the 1st of the month. In the case of the start day and month being missing, the date will be imputed with 01 January.

  The duration of ITP (years) will be calculated as follows, where Date of Screening is from the parent study, and the date of diagnosis will be obtained from the ITP history page of the eCRF:

  $\frac{\text{Date of screening} - \text{Date of Diagnosis}}{365.25}$

- The duration of ITP will be presented in the listings as follows:
  - In years to 1 decimal place for chronic primary ITP participants
  - In months (3-12) for persistent primary ITP participants
- The definition of Past and Prior ITP medications for this summary refers to the definition outlined in Section 6.5.

- Unique Prior ITP is derived as follows:
  - To derive prior ITP medications, see Section 6.5.
  - To derive unique: count all medications with ATC code [redacted] as one, count all medication with ATC code [redacted] as one, for remaining prior ITP medications count all unique standardized medication names (CMDECOD)

6.2.2 Lifestyle

A listing of lifestyle for DILI CRFs (DILI patients only) data (alcohol use and illicit drug use in the past six months (yes/no)) will be created using the SS.

6.3 Previous and ongoing medical history

Any medical conditions that were not reported in TP0003/TP0006 will be captured on eCRF of this study and listed using the ES.

6.4 Procedure history and concomitant medical procedures

Procedure history that was not reported in TP0003/TP0006, and concomitant medical procedures will be listed using the ES.

6.5 Concomitant medications

Medications will be classified as follows based on imputed start and stop date & times as outlined in Section 4.1.3. For the following definitions, the first administration of IMP refers to first administration of IMP in TP0004, unless otherwise noted.

Past Medications: defined as any medications that started and stopped before first administration of IMP.

This includes medications reported in the following eCRF pages:

- "ITP Treatment history"
- "Prior and Concomitant Medications", if end date before first IMP date
- "Prior and Concomitant Medications ITP Treatment", if end date before first IMP date.

Prior Medications: defined as any medications that started before the first administration of IMP.

This includes medications reported in the following eCRF pages:

- "ITP Treatment History",
- "Prior and Concomitant Medications", if start date before first IMP date.
- "Prior and Concomitant Medications ITP Treatment", if start date before first IMP date.

Prior and Concomitant (Baseline) Medications: defined as any medications that started prior to first administration of IMP and stopped after the first administration of IMP (classified as prior and concomitant medications). This includes medications reported in the following eCRF pages:

- "Prior and Concomitant Medications", if start date before first IMP date and end date after first IMP date or ongoing
- "Prior and Concomitant Medications ITP Treatment", if start date before first IMP date and end date after first IMP date or ongoing

Concomitant medications: defined as any medication that has been taken at least once after the first administration of IMP.

This includes medications reported in the following eCRF pages:

- "Prior and Concomitant Medications", if end date after first IMP date or ongoing
- "Prior and Concomitant Medications ITP Treatment", if end date after first IMP date or ongoing

Concomitant only medication: defined as any medication that started after first administration of IMP

This includes any medication reported in the following eCRF pages:

- "Prior and Concomitant Medications", if start date after first IMP date

"Prior and Concomitant Medications ITP Treatment", if start date after first IMP date.

Table 6-1: Concomitant Medications Classificationbelow summarizes concomitant medication classification with details around medication start and finish.

Table 6-1:Concomitant Medications Classification

Medication Started	Medication finished	Classification
Before 1st Dose IMP	Before 1st Dose IMP	Past
Any time	After 1st Dose IMP	Concomitant
After 1st Dose IMP	After 1st Dose IMP	Concomitant Only
Before 1st Dose IMP	After 1st Dose IMP	Prior and Concomitant (Baseline)
Before 1st Dose IMP	Any time	Prior Medications

All the categories mentioned above will be summarized separately for ITP medications; Non-ITP medications will be listed only (using the ES) to display the number and percentage of participants in each category by Anatomical Therapeutic Chemical (ATC) class, presenting as Anatomical Main Group (ATC Level 1), Pharmacological Subgroup (ATC level 3), Preferred Term (PT). Concomitant and Concomitant Only medications will be summarized by dosing regimen.

Any medications with missing dates and/or times will be handled as described in Section 4.1.2 to classify them as prior and/or concomitant.

Listings for ITP and Non-ITP medications will be also produced using the ES.

Note: WHODD Mar2021 will be used for ATC terms.

6.5.1 Assignment of medications to treatment period

The following rules will be used to assign a concomitant medication to a study period:

- **Treatment Period:** a medication is taken at least once between the first administration of IMP on Day 1 and [redacted] after the last dose of IMP (on Week 55) or the early withdrawal visit, for participants who were on [redacted] dosing at the end of the study. For participants who were on [redacted] dosing at the end of the study, the end date of the treatment period is [redacted] after the last dose of IMP, on Week 53.
- **Safety Follow-Up Period:** A medication will be assigned to the Safety Follow-Up Period if it has been taken at least once from the day after the end of the Treatment Period up until the EOS visit.

6.6 Prohibited concomitant medications and rescue medication

6.6.1 Prohibited concomitant medication

All prohibited concomitant medication listed in Section 6.4.2 in the protocol, will be summarized using the number and percentage of study participants who received prohibited concomitant medication by ATC class, presenting ATC Level 1, ATC level 3, and PT, ordered alphabetically for the ATC class and in terms of decreasing frequency for PT within ATC class using the ES by dosing regimen and overall. In the event of ties, PT will be ordered alphabetically.

6.6.2 Rescue Therapy

All rescue therapies mentioned in Section 6.4.3 in the protocol, identified if Rescue Medication is ticked as yes on eCRF, will be summarized using the ES.

The number and percentage of study participants who received rescue medication will be displayed by ATC class, presenting ATC Level 1, ATC level 3, and PT (ordered alphabetically for the ATC class and in terms of decreasing frequency for PT within ATC class using the ES, overall and by dosing regimen. In the event of ties, PT will be ordered alphabetically.

7 MEASUREMENTS OF TREATMENT COMPLIANCE

Not applicable. The number of infusions will be recorded as detailed in Section 8.6.

8 SAFETY ANALYSES

All safety analyses will be presented separately using the SS, unless otherwise noted. Listings will be presented using the SS by participant; tabulations will be presented by Treatment and Safety Follow-Up Period (refer to Section 3.2.2 for study period definitions). Summaries by be presented by whether the assessment occurred while the participant was receiving [redacted] or [redacted] dosing of rozanolixizumab at the time of the event or assessment. Listings will include a flag indicating whether the the participant was receiving [redacted] or [redacted] dosing of rozanolixizumab at the time of the event or assessment. Because some participants switched from [redacted] to [redacted] dosing, the N for all participants may differ from the sum of the Ns for [redacted] and [redacted] participants.

For results disclosure on public registries (eg. ClinicalTrials.gov), treatment-emergent adverse events and treatment-emergent serious adverse events will be published.

8.1 Statistical analysis of the primary safety endpoints

8.1.1 Estimand Details and Attributes to be considered for the evaluation of the primary endpoints

The following estimand attributes will be used for all participants:

Treatment conditions: Fixed dose equivalent to [redacted] and approximately [redacted] either [redacted] or [redacted]. Analyses will be split based on dosing regimen at the time of the event.

1. **Population:** Adult Study Participants with Primary Immune Thrombocytopenia (ITP) who fulfill the inclusion / exclusion criteria according to the protocol
2. **Endpoints:** See Sections 8.2 for more details.

3. **Intercurrent Events:** See below.

Table 8-1: Intercurrent Events (ICE), Intercurrent Events Strategies (ICES) and Missing data Strategies for the analysis of the primary endpoint

Intercurrent Events (ICE)	ICE Strategy	Missing Data Strategy
a) Use of Rescue therapy from Baseline prior Week 54	**Treatment Policy.** All data will be reported as obseved regardless of intercurrent event.	All data available will be reported. Missing values will not be imputed or included in the analysis.
b) Withdrawal from study due to TEAEs		
c) COVID-19*		

*COVID-19 Impact category: Temporary discontinuation of study drug, Permanent discontinuation of study drug, Termination of study participation and Relationship to COVID-19: confirmed, suspected, general or other as recorded in the COVID-19 impact eCRF form.

4. **Population Summary:** All primary safety analyses will be based on the SS and will be summarized using descriptive statistics. Further details for adverse event summaries, laboratory evaluations, ECGs, and vital signs are elaborated in the sections below.

8.2 Adverse events

8.2.1 Data considerations

Adverse events will be recorded from the time of informed consent until study completion. All AEs will be coded (Section 3.7).

In addition, AEs will be classified according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 5 or later for severity. For any AEs where it is not possible to provide a CTCAE grading, the events will be assessed using a standard severity classification (mild, moderate, and severe). For the purpose of the tabulations, all CTCAE toxicity classifications will be mapped to a mild/moderate/severe grade as described below:

CTCAE Toxicity Grade: Severity

- Grade 1: Mild
- Grade 2: Moderate
- Grade 3, 4, 5: Severe
- Not gradable

In summaries including intensity, the categories will be summarized according to the following:

Grade: Intensity

- Grade 1: Mild
- Grade 2: Moderate
- Grade 3: Severe

For AEs that were not classified according to the CTCAE Toxicity (Severity) criteria, the standard intensity Grade will be applied. In case there are mismatches between Severity and Intensity Grade, the worst case (i.e., the most severe grade) will be applied.

Treatment-emergent AEs are defined as AEs starting after the time of first IMP administration up to and including 8 weeks (56 days) after the final dose.

AEs before first dosing and AEs after 8 weeks (56 days) following the final dose will be combined in one category and listed.

Where dates are missing or partially missing, AEs will be assumed to be treatment-emergent unless evidence exists that does not allow the AE to be treatment-emergent. Handling of missing dates for classification of AEs as TEAEs is described in Section 4.1.4 .

A Persistent AE is defined as an unresolved AE that extends continuously from TP0003/TP0006 and does not worsen in intensity or severity following exposure to IMP in TP0004. Persistent AEs will be recorded in the TP0004 database. If the intensity or severity of a persistent AE worsens it will be considered a new event and reported using the rules detailed below. The following rules will be used to assign a TEAE to a study period:

TEAE-Treatment Period: a TEAE will be assigned to the Treatment Period for the tabulations if the start date of the event is on or after the date of the first administration of IMP up to [redacted] following the final dose of IMP within the treatment period.

TEAE-Safety Follow-Up Period: a TEAE will be assigned to the Safety Follow-Up Period for the tabulations if the start date of the event is greater than [redacted] after the date of the final dose of IMP until 8 weeks following the final dose; events starting later than 8 weeks following the final dose of IMP are not considered TEAEs.

In the case of an AE leading to early withdrawal in the Treatment Period, a TEAE will be assigned to the Treatment Period based on the last received infusion plus [redacted] Subsequent TEAEs (up to 8 weeks post-last dose) will be assigned to the Safety Follow-Up Period.

AEs will be presented as "number of participants (percentage of participants) [number of events]". In this style of output, "[number of events]" will include all cases of an AE including repeat occurrences in individual participants, while "number of participants" will count each participant only once.

AE analysis will also be presented by the dosing regimen received at the start of the adverse event (either [redacted] or [redacted] dosing).

8.2.2 Adverse Event Summaries

The number and percentage of participants who experience AEs will be summarized separately by dosing regimen using the SS.

The following outputs will be created:

1. Incidence of TEAEs (defined as the number and percentage of participants with at least one TEAE (incidence proportion) – Overview. The following categories will be included by dosing regimen ([redacted] or [redacted]):
   - Any TEAEs
   - AESMs

- AESIs
- Serious TEAEs
- TEAEs leading to Study Discontinuation
- Permanent Withdrawal from IMP due to TEAEs
- Treatment-related TEAEs
- TEAEs with CTCAE Grade 3 and above [or rated as 'severe' for events with no CTCAE classification]
- All Deaths (AEs leading to death)
- All Deaths (TEAEs leading to death)
- TEAEs leading to dose modification (defined as TEAEs with an action taken with study medication of "dose increased" or "dose decreased"). This excludes withdrawal of IMP
- TEAEs resulting in temporary treatment interruption

The following summaries will be created by SOC, HLT and PT by dosing regimen ([redacted]) using the SS, unless stated otherwise:

2. Incidence of fatal TEAEs by relationship
3. Incidence of Serious TEAEs by Relationship
4. Incidence of TEAEs leading to Permanent discontinuation of IMP
5. Incidence of Non-serious TEAEs Above Reporting Threshold of 5% of participants by System Organ Class and Preferred Term

– AESIs are Potential Hy's Law, defined as ≥3xULN ALT or AST with coexisting ≥2xULN total bilirubin in the absence of ≥2xULN ALP, with no alternative explanation for the biochemical abnormality.

– AESMs are severe headache, severe GI disturbance (i.e., diarrhea, abdominal pain, vomiting), opportunistic infections, arterial and venous thrombotic and thromboembolic events.

– AESMs and AESIs will be identified based on the assessment by the Investigator as recorded in the CRF. An AE will be counted as an AESM if there is a 'yes' response to the question "Is this an event of Special Monitoring?" and 'no' otherwise. An AE will be counted as an AESI if there is a 'yes' response to the question "Adverse Event of Special Interest?" and 'no' otherwise.

Listings will be presented by dosing regimen, most recent dose, and participant for all AEs. This will include the onset date/time and outcome date/time of the event (including relative days), the AE duration, days since first dose of IMP, days since most recent dose of IMP, most recent dose, pattern of event, severity/intensity, relationship, action taken and outcome. In addition, the listing will flag AEs that led to discontinuation, TEAEs, serious adverse events (SAEs), AESMs, and AESIs. Most recent dose and dosing regimen will also be included.

AEs of Focus:

AEs of Focus will be defined using Version 3.0 or later of "Adverse Events of Focus for the Rozanolixizumab program". In addition, worsening thrombocytopenia and

haemorrhagic events will be included as AEOF as described in AEOF Version 1.4. The following AEs are defined in the Rozanolixizumab program as AEs of Focus (please see Appendix 13.1 for more details)

- Headaches
- Gastrointestinal Disturbances
- Hypersensitivity Reactions
- Anaphylactic Reactions
- Injection Site Reactions
- Infusion Reactions
- Opportunistic Infections
- Reductions in Albumin and Plasma Proteins
- Effects on the Kidney
- Drug Related Hepatic Disorders
- Thromboembolic Events
- Hemorrhagic Events
- Worsening of Thrombocytopenia

AEOFs will be listed only.

8.3 Vital Signs, Physical Findings, and Other Observations Related to Safety

8.3.1 Vital Signs and Physical Findings

The following vital signs measurements will be obtained:

- Pulse rate
- Systolic and diastolic blood pressure
- Temperature (oral, tympanic, or axillary)

A summary of participants who met each of the Marked Abnormality (MA) Criteria (Appendix 13.3) will be summarized separately by dosing regimen at each scheduled timepoint using the SS.

A by-participant listing of all vital sign measurements (defined in Section 3.3) will be presented for SS by timepoint. The listing will include a flag for values identified as MA criteria (Appendix 13.3). Dosing regimen will be included in the listing.

Repeated and unscheduled measurements will be handled as described in Section 4.2.

8.4 12-lead Electrocardiograms (ECG)

12-Lead ECG data (measured values and changes from Baseline as defined in Section 3.3) will be listed only.

The following variables will be reported:

- Heart rate
- PR interval
- RR interval
- QRS duration
- QT interval
- QT corrected for heart rate using Bazett's formula ($QTcB = QT/RR^{1/2}$)
- QT corrected for heart rate using Fridericia's formula ($QTcF = QT/RR^{1/3}$)

- A summary of participants who meet each of the Marked Abnormally (MA) criteria outlined in Appendix 13.4 will be summarized on the SS at each timepoint. Visits where triplicate ECGs were performed will be designated by a "*".

8.5 Clinical Safety Laboratory Assessments

Laboratory data (as specified in Table 10-1: Protocol-required safety laboratory assessments in the protocol) and changes from Baseline (if applicable) for numeric variables will be listed separately by participant and timepoint using the SS. Baseline will be the pre-dose value obtained at the Visit 1 (Week 1 Day 1) result. Values outside the reference range for the numeric variables will be flagged in the listings. The reference ranges will also be reported in the listings. In addition, the listings will include a flag for values identified as Laboratory assessments – MA Criteria (Appendix 13.2).

Measurements BLQ will be imputed with half of the LLOQ for the purpose of calculating change from Baseline. Measurements ALQ, if applicable, will be imputed to the upper quantification limit. These rules will be applied to all safety laboratory data including clinical chemistry and urinalysis.

Descriptive statistics will be calculated if at most 1/3 of the individual data points at a time point are missing or are either not quantifiable (<LLOQ) or ALQ. Values that are BLQ will be replaced by the numerical value of the LLOQ/2 in this instance and values that are ALQ will be imputed to the value of the upper quantification limit. If more than one-third of the individual data points at a timepoint are missing or not quantifiable (BLQ and/or ALQ), no descriptive statistics will be calculated.

The following summaries/tables will be created:

- A summary of all participants who met each of the Laboratory assessments – MA criteria (Appendix 13.2) will be summarized by dosing regimen (using SS) at each timepoint.

A listing for laboratory assessments will be also created using the SS. The listing will include dosing regimen.

8.5.1 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 listed separately by participant and visit using the SS to include:

- Subjects with at least one post-Baseline liver laboratory assessment
- Incidence of potential hepatotoxicity with symptoms potentially associated with hepatitis or hypersensitivity, which will account for the number and percentage of subjects meeting laboratory criteria for pDILI for at least 1 visit and reporting at least 1 symptom potentially associated with hepatitis or hypersensitivity according to the Investigator on the pDILI CRF)
- Incidence of potential hepatotoxicity with no symptoms potentially associated with hepatitis or hypersensitivity, which will account for the number and percentage of subjects meeting laboratory criteria for pDILI for at least 1 visit and not reporting any symptom potentially related to hepatitis or hypersensitivity according to the Investigator on the pDILI CRF
- Number and percentage of study participants who meet the Laboratory criteria for pDILI (see Table 8-2 below).

Table 8-2: Laboratory criteria for pDILI

Laboratory Criteria	Comments
(AST or ALT > 3 x ULN) and TBL > 1.5 x ULN (AST or ALT > 3 x ULN) and TBL > 2 x ULN	- All values must be met at the same sample taken from the same visit
(AST or ALT > 3 x ULN) and TBL > 2 x ULN and ALP < 2 x ULN	- All values must be met at the same visit - To be counted as potential Hy's Law, all criteria must be met at the same sample taken from the same visit.

ALT = Alanine aminotransferase; AST = Aspartate aminotransferase; TBL = total bilirubin; ULN = upper limit of normal range.

A listing will be created of 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. The listing will specify AST, ALT, TBL, and ALP.

8.6 Extent of exposure

The following summary will be created overall and for each dosing regimen using the SS separately:

a) Study IMP duration and Subject-Years of Time at Risk using descriptive statistics, the total of IMP duration (subject-years, which is a subset of total time at risk excluding non-treated periods) and total time at risk (subject-years). In all calculations, if the participant dies and the date of death is missing, the date of death can be imputed as the date of last infusion of the treatment the participant was taking.

   - The number of days on IMP (extent of exposure), will be summarized using descriptive statistics for the overall treatment period.

The number of days on IMP will be calculated as follows:

Number of days on IMP = [(Date of Last Dose Received) - (Date of First Dose Received)] + 1

The number of days on [redacted] dosing will be calculated as follows:

Number of days on IMP = [(Date of Last [redacted] Dose Received) - (Date of First [redacted] Dose Received)] + 1

The number of days on [redacted] dosing will be calculated as follows:

Number of days on IMP = [(Date of Last [redacted] Dose Received) - (Date of First [redacted] Dose Received)] + 1

In all calculations, if a patient dies and the date of death is missing, the date of death can be imputed as the date of last infusion of the treatment the participant was taking.

- Subject-Years of Time at Risk:
  - For study participants who complete the study as planned and continue into the MAP (Managed Access Program), and therefore do not have the SFU visit in the parent study

    Date of last visit – Date of first dose + 1
  - For study participants who die prior to the final visit

    Date *of death – Date of first dose + 1*
  - For all other study participants, use the minimum of the following:

    Date of last dose – Date of first dose + 56

    Or

    Date of last clinical contact – Date of first dose + 1
  - This last group could include study participants who discontinue early or study participants who are ongoing in the SFU period at the time of the data snapshot.
- Subject-Years of Time at Risk for [redacted] Dosing
  - For study participants who do not switch to [redacted] dosing, time at risk for [redacted] dosing is the same as total time at risk
  - For study participants who switch to [redacted] dosing, time at risk for [redacted] dosing is

    Date of First [redacted] Dose Received - Date of First [redacted] Dose Received + 1
- Subject-Years of Time at Risk for [redacted] Dosing
  - For study participants who do not switch to [redacted] dosing, time at risk for [redacted] dosing is zero days

- For study participants who complete the study as planned and continue into the MAP, and therefore do not have the SFU visit in the parent study

  Date of last visit – Date of first [redacted] *dose + 1*

- For study participants who die prior to the final visit

  Date *of death – Date of first* [redacted] *dose + 1*

- For all other study participants, use the minimum of the following:

  Date of last dose – Date of first [redacted] *dose + 56*

  Or

  Date of last clinical contact – Date of first [redacted] *dose + 1*

- This last group could include study participants who discontinue early or study participants who are ongoing in the SFU period at the time of the data snapshot.

- The total time at risk is calculated as the sum of the person-time at risk (days) across all participants in the population divided by 365.25.

As described in the protocol, fixed-unit doses across body weight tiers and dosing regimen will be employed in this study according to the following scheme, as presented in Table 8-3.

Table 8-3: TP0004 dose levels and weight tiers of rozanolixizumab

Dose eqv / Bodyweight	[redacted] Dose level 1	Dose level 2	[redacted] Dose level 3
>35 to <50kg	[redacted]	[redacted]	No weight adjustment [redacted]
≥50 to <70kg	[redacted]	[redacted]	
≥70 to <100kg	[redacted]	[redacted]	
≥100kg	[redacted]	[redacted]	

eqv=equivalent

If a study participant is in the lowest body weight tier (below 50kg) and is on the lowest dose level with a platelet count between $>150\times10^9$/L and $<400\times10^9$/L, the investigator might decide to temporarily stop treatment according to medical judgement based on the observation of platelet variability. If the platelet count increases above 400×10^9/L then treatment must be stopped anyway.

A listing with all drug administration details including date, start and stop time of infusion, interruptions, discontinuations, dose, volume delivered, percent of planned dose and reasons for any interruptions or discontinuations will be created using the SS.

8.7 Concentrations of Total Protein & Albumin

Concentrations of total protein and albumin for each visit (as described in the schedule of events in the protocol) will be listed using the SS.

8.8 Serum and Plasma Complement Levels

Serum (C3 and C4) and plasma (C3a and C5a) complement variables will be listed by time point.

Measurements below the limit of quantification (BLQ) will be imputed with half of the lower limit of quantification (LLOQ). Measurements above the limit of quantification (ALQ), if applicable, will be imputed to the upper limit of quantification.

All analyses described in this section will be performed on the SS.

8.9 Other Safety Variables

8.9.1 Physical examination

Results of physical examination abnormalities will be listed.

8.9.2 Pregnancy testing

The pregnancy test will be a urine pregnancy test at all visits as per schedule of assessments. If the urine pregnancy test is positive, then a confirmatory serum pregnancy test is required.

A by-participant listing of the pregnancy test data will be provided for the SS.

8.9.3 Childbearing potential

Childbearing potential will be collected at Baseline. A by participant listing will be provided for all the participants enrolled.

8.9.4 Assessment and management of Tuberculosis

Results of the interferon-gamma release assay tuberculosis (TB) test will be listed.

Results of the chest X-ray for TB will be listed.

Results of TB signs and symptoms questionnaire will be listed.

8.9.5 COVID-19 Impact

A listing of impact of COVID-19 pandemic for any reason (including impact category and visit (timepoint)) by dosing regimen using the ES will be created.

9 EFFICACY ANALYSES

Data will be listed, and for continuous variables, descriptive statistics will be generated for the observed values and changes from Baseline. For categorical variables, frequency counts and percentages will be presented.

All summary outputs for the secondary efficacy endpoints will be presented by visit, and by the treatment received in the parent studies (TP0003/TP0006) .

The following estimand attributes will be used for all participants

1. **Treatment conditions:** Fixed dose equivalent to [redacted] and approximately [redacted] either [redacted] or [redacted] based on body weight tiers.

2. **Population of Interest:** Adult Study Participants with Primary Immune Thrombocytopenia (ITP) who fulfill the inclusion / exclusion criteria according to the protocol

The remaining Estimand Attributes are presented below for each efficacy endpoint.

9.1 Statistical analysis of the secondary efficacy endpoints

9.1.1 Stable Clinically Meaningful Response

The secondary efficacy endpoint will be analyzed according to the following Estimand Attributes:

3. **Endpoint:** Stable Clinically Meaningful Response, defined as Clinically Meaningful Response (ie, platelet count $\geq 50 \times 10^9$/L) without rescue therapy at ≥70% of the visits over the planned 52 week Treatment Period starting at Week 4
4. **Intercurrent Events:** see below.

Table 9-1: Intercurrent Events (ICE), Intercurrent Events Strategies (ICES) and Missing data Strategies for the analysis of the secondary efficacy endpoint

Intercurrent Events (ICE)	ICE Strategy	Missing data strategy
a) Use of Rescue therapy from Baseline prior Week 54	A composite strategy Participants impacted by any ICE (a, b, c and d) will be considered as non-responders starting from the time of event.	Not applicable
b) Participants who experience any TEAEs leading to permanent treatment discontinuation		
c) Participants who discontinue prior to receiving IMP		
d) Participants who do not have any post-treatment assessment		
e) COVID-19*	A composite strategy Participants impacted by ICE (e) will be considered as non-responders at the time of event.	

* COVID-19 Impact category: Temporary discontinuation of study drug, Permanent discontinuation of study drug, Termination of study participation and Relationship to COVID-19: confirmed, suspected, general or other as recorded in the COVID-19 impact eCRF form.

5. **Population-level summary:** Owing to early termination of the study, the population-level summary will be provided using descriptive statistics.

The following efficacy endpoints will be analyzed using the SS and will follow the same considerations for treatment condition and population of interest from Section 9.1 above.

9.1.2 Change from Baseline to Week 53 or 55 for ITP-PAQ Symptoms domain score

3. Change in ITP-Patient Assessment Questionnaire (ITP-PAQ, see section 8.1.3.1 in the protocol for details) Symptom score will be calculated at week 53 or 55 relative to the

Baseline and will be limited to the participants with a Baseline ITP-PAQ score available. Please see Section 13.5 for details about ITP-PAQ scoring and ITP-PAQ scales. Summary will be by dosing regimen. Week 53 will be used for participants who finished the study on [redacted] dosing, and week 55 will be used for participants who finished the study on [redacted] dosing. The intercurrent event strategy is as follows:

4. **Intercurrent Events:** see below.

Table 9-2: Intercurrent Events (ICE), Intercurrent Events Strategies (ICES) and Missing data Strategies for the analysis of Change from Baseline to Week 53 or 55 for ITP-PAQ Symptoms domain score

Intercurrent Events (ICE)	ICE Strategy	Missing data strategy
a) Use of Rescue therapy from Baseline prior Week 53 or 55	A composite strategy Participants impacted by any ICE (a, b, c and d) will be considered as non-responders starting from the time of event and change from baseline to week 53 or 55 will be set to 0.	In case of missing ITP-PAQ assessment at Baseline or week 53 or 55, this endpoint will be set to blank
b) Participants who experience any TEAEs leading to permanent treatment discontinuation		
c) Participants who discontinue prior to receiving IMP		
d) Participants who do not have any post-treatment assessment		
e) COVID-19*	A composite strategy Participants impacted by ICE (e) will be considered as non-responders at the time of event. If ICE occurs at week 53 or 55, change from baseline to week 53 or 55 will be set to 0.	

5. **Population-level summary:** Owing to early termination of the study, the population-level summary will be provided using descriptive statistics.

9.2 Statistical analysis of the other efficacy endpoints

9.2.1 Mean Change from Baseline in platelet count at each visit

Mean Change from Baseline (as collected on TP0004 Visit 1/BL) in platelet count at each visit will be summarized separately on the SS using descriptive statistics at each timepoint. Summaries will be presented by treatment received during the parent study (TP0003/TP0006), either rozanolixizumab or placebo. Summary will be by dosing regimen. The ICE strategy will be as follows:

Table 9-3: Intercurrent Events (ICE), Intercurrent Events Strategies (ICES) and Missing data Strategies for the analysis of Mean Change from Baseline in platelet count at each visit

Intercurrent Events (ICE)	ICE Strategy	Missing data strategy
a) Use of Rescue therapy from Baseline prior Week 53 or 55	A while-on-treatment strategy Participants impacted by the ICE (a) will be excluded from summaries and change in baseline starting from the time of the event.	Not applicable

9.2.2 Clinically Meaningful Response at each visit

Clinically meaningful response at each visit will be summarized on the SS at each timepoint. Summaries will be presented by treatment received during the parent study (TP0003/TP0006), either rozanolixizumab or placebo. Summary will be by dosing regimen. The ICE strategy will be as follows:

Table 9-4: Intercurrent Events (ICE), Intercurrent Events Strategies (ICES) and Missing data Strategies for the analysis of Clinically Meaningful Response at each visit

Intercurrent Events (ICE)	ICE Strategy	Missing data strategy
b) Use of Rescue therapy from Baseline prior Week 53 or 55	A while-on-treatment strategy Participants impacted by the ICE (a) will be excluded from summaries and change in baseline starting from the time of the event.	Not applicable

9.2.3 ITP-BAT bleeding events and severity by visit

ITP-BAT bleeding events and severity by visit, will be listed on the SS. Dosing regimen will be included in the listing.

Table 9-5: ITP-specific Bleeding Assessment Tool (ITP-BAT) Domains and categories

	Skin	Mucosal	Organ

- Petechiae - Ecchymoses - Subcutaneous Hematomas - Bleeding from Minor Wounds	- Epistaxis - Oral cavity [a] - Subconjunctival Hemorrhage	- Gastrointestinal Bleeding Not Explained by Visible Mucosal Bleeding or Lesion - Lung Bleeding - Hematuria - Menorrhagia - Intramuscular Hematomas - Hemarthrosis - Ocular Bleeding - Intracranial Bleeding - Other Internal Bleedings

[a] Includes gum bleeding, hemorrhagic bullae or blisters, bleeding after bites to lip & tongue or after deciduous teeth loss

Notes:

- Presence of bleeding will be indicated by a Mucosae or Organs Grade ≥1, or Skin Grade ≥2.
- Bleeding reported by the participant without medical documentation will be graded 1.
- Fatal bleeding will be graded 5.
- Within each domain, the same grade is assigned to bleeding manifestations of similar clinical impact.
- The "worst" bleeding manifestation since the last visit will be graded, and the highest grade within each domain will be recorded.

Please see Section 13.6 ITP bleeding score for more details.

10 PHARMACOKINETICS (PK) AND PHARMACODYNAMICS (PD)

10.1 Pharmacokinetic endpoints

10.1.1 Plasma Concentration of Rozanolixizumab

Individual plasma concentration of Rozanolixizumab will be summarized by scheduled sampling day for the PK-PPS using n, arithmetic mean, median, SD, minimum, maximum, geometric mean (geomean), geometric coefficient of variation (geoCV) and 95% CI (assuming log-normally distributed data) overall. The following sample exclusions will be applied in the summary:

1. If dose is missed – the next predose PK sample 2 weeks after would be impacted and is excluded.
2. If dose is given >=3 days out of allowed window (that would be 5 days out in total as visit window is typically ±2 days) after what it should be given – the current predose PK sample if it is also delayed and the next predose sample if taken at the per protocol planned time and it is not readjusted based on dosing, could be impacted and thus we would exclude it.
3. If dose is given >=3 days out of window (that would be 5 days out in total) before what it should be given – the PK predose sample of the impacted dosing visit and the next

predose PK sample if taken at the per protocol planned time and it is not readjusted based on dosing, could be impacted and thus we would exclude it.

4. If dose is given at the right time but next PK visit is impacted by >=3 days out of the window, then the next PK visit is the one impacted and excluded
5. For weeks 13 and 23 if a postdose PK sample 1 to 5 days is taken, if the postdose sample is not taken within 1 to 5 days post actual dose, then it would need to be excluded.
6. For PK samples on Day 3, Day 5, and Day8, if outside window then exclude from table.

The following rules will apply for PK data listings and summaries:

- Values below the LLOQ will be reported as below the limit of quantification (BLQ)
- Descriptive statistics of concentrations will be calculated if at most 1/3 of the individual data points at a timepoint are missing or are not quantifiable (<LLOQ). Values that are BLQ will be replaced by the numerical value of the LLOQ/2 in this instance.
- The 95% CI lower and 95% CI upper should be left blank if the SD (or equivalently, the geoCV) is 0
- The geoCV will be calculated using the following formula where SD is the standard deviation from the log-transformed data

$$\text{geoCV (\%)} = \text{sqrt}[(\exp(\text{SD}^2) - 1)] \times 100$$

Individual concentrations of rozanolixizumab will be listed for the RS for each individual with the actual time and will include the equivalent dose and actual dose being administered previous to the pk sample, the sampling time in days relative to the previous dose, the IgG observed at the same visit, the ADA titer observed for the binding assay and the NAb titer for the same visit and platelet count for the corresponding visit.

10.2 Antidrug Antibodies (ADA)

The immunogenicity analysis will be done on the SS.

Anti-rozanolixizumab antibodies will be measured using a three-tiered assay approach: screening assay, confirmatory assay and titration assay. Samples will first be evaluated in the screening assay (reported as 'negative screen' or 'positive screen'), followed by analysis of screened positive samples in the confirmatory assay to confirm the true positivity of the samples (reported as 'negative immuno-depletion' or 'positive immuno-depletion'). Samples that are confirmed as positive in the confirmatory assay 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)). Any sample confirmed positive for ADA within the confirmatory assay will be further evaluated for the presence of neutralizing anti-rozanolixizumab antibodies.
Screening, confirmatory, and titer cut points of the respective assays will be determined by the bioanalytical laboratory. The relevant statistical reports will be provided as part of the bioanalytical reports. Rozanolixizumab has the potential to interfere with the antibody assay at concentrations above the drug tolerance limit (DTL); therefore, an integrated evaluation of anti-rozanolixizumab antibody results and rozanolixizumab plasma concentration will be used to enable the interpretation of immunogenicity results. The ADA sample status will be determined for each visit where samples were taken for ADA analysis:

- Sample values that are either 'negative screen' or the combination of 'positive screen' and 'negative immunodepletion', will be defined as ADA negative if corresponding rozanolixizumab concentrations are equal or below the validated drug tolerance limit of the ADA assay [redacted] rozanolixizumab) allowing detection of 100ng/mL ADA
- Sample values that are either 'negative screen' or the combination of 'positive screen' and 'negative immuno-depletion', but with corresponding rozanolixizumab concentrations above the validated drug tolerance limit of the ADA assay, will be defined as ADA inconclusive
- Sample values that are 'positive screen' and 'positive immunodepletion' will be defined as ADA positive
- Samples that could not be tested for ADA status due to inadequate sample volume, mishandling, or errors in sample collection, processing, storage, etc., will be defined as Missing
- Neutralizing antibody (NAb) sample status (positive/negative/missing) will be determined for ADA positive samples. Samples that are NAb positive will be evaluated in a titration assay to quantify the NAb level and will be reported as titer.

The ADA participant status will be classified on individual and group level as outlined below (Shankar et al. 2014; Rup et al, 2015). Individual study participants will be assessed for ADA participant status, composed of 6 categories: ADA negative, inconclusive, and ADA positive, whereby a positive participant's status is determined as originating from a treatment-induced, boosted, reduced or unaffected ADA response.

Study participants who are identified as being treatment-induced or treatment-boosted ADA-positive will be grouped as treatment emergent (TE)-ADA positive participants. Study participants who are identified as being treatment-reduced or treatment-unaffected ADA-positive will be grouped as non-TE-ADA positive participants. Both TE-ADA positive and non-TE–ADA positive participants will be further classified as NAb negative or NAb positive.

The individual and combined ADA participant categories will be summarized overall through the SFU sample if applicable (timepoint of interest). The ADA categories are defined in Table 10-1.

Notes:

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

ADA Baseline

By default, the Day 1 of the parent study will be the Baseline value if the ADA status at screening (from parent study) is ADA negative or missing. If the ADA status at screening of the parent study is ADA positive and ADA status at Day 1 of parent study is ADA negative or missing, the screening will be the Baseline value. If the ADA status at screening and Day 1 (of the parent study) are same, Day 1 will be the Baseline value. For participants stratified to placebo in the parent study the Baseline value from TP0004 will be used.

Table 10-1: Terms and Definitions for ADA Status Evaluation in Study Participants

Term	Definition	Category
Individual participant categories		
Pre-ADA negative – treatment induced ADA negative (ADA-NEG)	Study participants who have an ADA negative sample at Baseline and at all sampling points post-Baseline up to the timepoint of interest.	1
Inconclusive	Study participants who have an ADA positive or negative Baseline sample and some post-Baseline samples are missing or inconclusive, while other post-Baseline samples are ADA negative up to the timepoint of interest.	2
Pre-ADA negative – treatment induced ADA positive (TI-POS)	Study participants who have an ADA negative sample at Baseline and at least one ADA positive sample at any sampling point post-Baseline up to the timepoint of interest	3
Pre-ADA positive – treatment boosted ADA positive (TB-POS)	Study participants who have an ADA positive sample at Baseline and at least one ADA positive sample at any sampling point post-Baseline up to the timepoint of interest, with increased titer values compared to Baseline (greater than a predefined fold difference increase from Baseline value which will be defined within the validation of the assay ie MSR of the assay[1])	4
Pre-ADA positive – treatment reduced ADA positive (TR-POS)	Study participants with an ADA positive sample at Baseline, and ADA negative samples at all sampling points post-Baseline up to the timepoint of interest	5
Pre-ADA positive – treatment unaffected ADA positive (TU-POS)	Study participants with an ADA positive sample at Baseline and an ADA positive sample at any sampling point post-Baseline up to the timepoint of interest, with titer values of the same magnitude as Baseline (less than a predefined fold difference from the Baseline value which will be defined within the validation of the assay, ie MSR of the assay[1])	6
Combined participant categories		
Treatment emergent ADA positive (TE-POS)	Includes study participants who are treatment induced ADA positive (category 3) or treatment boosted ADA positive (category 4).	7
Non-treatment emergent ADA positive (Non-TE-POS)	Includes study participants who are treatment reduced ADA positive (category 5) or treatment unaffected ADA positive (category 6).	8
Treatment emergent ADA positive – NAb positive (TE-POS, NAb-POS)	Includes study participants who are treatment emergent positive (category 7) and have at least one NAb positive sample	9

Table 10-1: Terms and Definitions for ADA Status Evaluation in Study Participants

Term	Definition	Category
Treatment emergent ADA positive – NAb negative (TE-POS, NAb-NEG)	Includes study participants who are treatment emergent positive (category 7) and have no NAb positive samples	10
Non-treatment emergent ADA positive - NAb positive (Non-TE-POS, NAb-POS)	Includes study participants who are non-treatment emergent positive (category 8) and have at least one NAb positive sample	11
Non-treatment emergent ADA positive - NAb negative (Non-TE-POS, NAb-NEG)	Includes study participants who are non-treatment emergent positive (category 8) and have no NAb positive samples	12

[1] The fold difference increase from baseline value, ie, the minimum significant ratio (MSR) determined during assay validation, will be reported in the relevant tables, listings and figures. It reflects the fold difference in titer level that considered higher than the assay variation in titer determination. The MSR is equal to 1.86.

The following outputs will be created:

Summaries by dosing regimen, using SS:

Tables:

- Number and percentage of participants with positive, negative, inconclusive, or missing sample ADA status at the time of each visit and will be summarized overall. Denominator is the number of study participants having a non-missing result at that visit. Summary will be by dosing regimen.
- Number and percentage of participants in each of the ADA participant individual categories (1 to 6) and combined (7-12) presented above will be summarized overall. Denominator will be the total number of study participants having an individual ADA participant category defined
- Summary tables displaying the total prevalence of pre-existing ADA and NAb, and persistent ADA positivity, as defined below:
  - Total prevalence of pre-existing ADA and NAb: number and percentage of participants having an ADA positive sample status at baseline of the parent study, with the denominator being the total number of study participants having a non-missing sample result at baseline, by treatment group in the parent study and overall. The same will be repeated for NAb.
  - Persistent ADA positivity: Number and percentage of study participants with treatment-induced ADA positive samples detected at 2 or more sequential sampling time points during the treatment (including observation and off-treatment periods), where the first and last ADA positive samples are separated by at least 16 weeks (equal to 5 half-lives of human IgG [22 days], as per Rup et al., 2015), by treatment group in the parent study and overall.

Listings:

Listings by timepoint by dosing regimen using the SS will be created. The following datapoints will be included:

- Rozanolixizumab concentration
- Total IgG, and absolute platelet counts
- ADA screening results (with the confirmatory result, the ADA titer result if applicable and the ADA sample status)
- NAb result titer (when performed)
- Time since administration of IMP (in days)
- Individual ADA participant classification that apply (as defined above)
- Previous visit actual dose (mg/kg equivalent) and actual dose (mg)
- By-subject listing of all TEAEs, including the time of onset, the ADA and NAb sample status and ADA and NAb titers at the closest sampling time point prior to and subsequent to the TEAE, and time since last administration of IMP (in days).

10.3 Pharmacodynamic endpoints

The following pharmacodynamic endpoints will be summarized separately on the SS.

10.3.1 Change from Baseline in Total Serum IgG concentration over time

Total serum IgG concentrations will be summarized and listed on the SS by time point for absolute values, change from Baseline, and percentage change from Baseline. Dosing regimen will be included in the listing.

10.3.2 Change from Baseline in IgG subclasses concentration over time

IgG subclasses will be listed on the SS by time point for absolute values, change from Baseline, and percentage change from Baseline overall and stratified by body weight tier. Stratification by region may be also performed. Dosing regimen will be included in the listing.

10.3.3 Serum IG concentrations (IgA, IgE, IgM) over time

Immunoglobulins (IgE, IgA and IgM) will no longer be summarized; IgE, IgA and IgM concentrations will be listed only. Dosing regimen will be included in the listing.

10.4 Influence of Rozanolixizumab on vaccination titers

10.4.1 Vaccination titers against *Streptococcus pneumoniae, Neisseria meningitidis,* and *Haemophilus influenzae* in splenectomized study participants

Vaccine specific antibodies concentrations will be listed to capture absolute values in vaccination titers against *Streptococcus pneumoniae, Neisseria meningitidis*, and *Haemophilus influenzae* in splenectomized study participants by visit using the SS.

10.5 Effect of Rozanolixizumab on post-vaccination biomarker(s) in study participants who received COVID-19 Vaccine

For study participants who receive the COVID-19 vaccination, post-vaccination biomarkers will be listed (using the SS) for vaccination samples in those study participants that were vaccinated by all pertaining visits.

11 OTHER ANALYSES

11.1 Statistical analysis of other endpoints

11.1.1 Effect of Rozanolixizumab on study participant perceived symptoms

11.1.1.1 ITP-PAQ V1 Domain Score

The ITP-PAQ V1 consists of 44 items that comprise 10 scales. Each of the 10 scales is scored 0 to 100, with higher scores indicating better quality of life. Four of the scales measure physical health: Symptoms, Bother, Fatigue, and Activity. Two of the scales measure emotional health: Fear and Psychological Health. The remaining four scales measure other aspects of QOL: Work QOL, Social QOL, Women's Reproductive QOL, and Overall QOL.

A by-subject listing of the ITP-PAQ V1 questionnaire, ITP-PAQ V1 item responses will be provided for using the SS. The listing will include dosing regimen.

11.1.2 Reduction in use of steroids in study participants

11.1.2.1 Percent change in oral steroid dose over time

The oral steroid dose will be listed at each timepoint from Week 1 to Week 53 or 55 as available depending under which protocol version the patient completed the study. Only one steroid dose should be selected between each dose; the start date should be before the timepoint, and the end date should be the same day or later than the timepoint.

11.1.2.2 Change in dose and/or frequency of concomitant ITP medications

Dose of permitted concomitant ITP medications (as defined in Protocol Table 6-2) from Week 1 to Week 52 will be listed as available.

11.2 Statistical analysis of other exploratory endpoints

All exploratory variables will be listed by visit unless otherwise stated. No inferential assessments or confirmatory statistical tests will be performed. Descriptive statistics will be generated for the observed values and the change from Baseline for all continuous outcomes. For categorical variables, frequency counts and percentages will be presented. Dosing regimen will be included in all listings.

11.2.1 Effect of Rozanolixizumab on Patient Reported Outcomes (PRO)

11.2.1.1 FATIGUE-PRO physical fatigue score

The Fatigue Patient Reported Outcome (PRO) physical fatigue instrument consists of 9 items. The scale is 1 out of the 3 scales composing the broader Fatigue instrument developed by UCB. Items are rated within a 7-day recall period on a 5-point Likert frequency scale ranging from "none of the time" to "all of the time."

A by-subject listing of the FATIGUE-PRO items will be provided using the SS for all participants.

11.2.1.2 Patient Global Impression of Severity (PGI-S)

The PGI-S consists of a single-state, self-report measure that rates a study participant's severity of specific condition, depicting a study participant's rating of overall symptoms ("none" , "mild", "moderate", "severe", or "very severe").

A by-subject listing of PGI-S will be provided using the SS for all participants. Dosing regimen will be included in the listing.

11.2.1.3 Patient Global Impression of Change (PGI-C)

The PGI-C is a single-state, self-report measure that reflects a study participant's belief about the efficacy of treatment for a specific condition, on a 7-point scale depicting a study participant's rating of overall improvement ("very much improved", or "much improved", "minimally improved" , "no change", "minimally worse", "much worse", or "very much worse"). Dosing regimen will be included in the listing.

A by-subject listing of PGI-C will be provided using the SS for all participants . Dosing regimen will be included in the listing.

11.2.2 Effect of Rozanolixizumab on Health-Related Quality of Life (HRQoL)

11.2.2.1 European Quality of Life-5 Dimensions, 5 Levels Assessment (EQ-5D-5L)

As described in section 8.5.3.4 in the protocol, the EQ-5D-5L health questionnaire consists of 2 pages: the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS).

The descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The patient is asked to indicate his/her health state by ticking the box next to the most appropriate statement in each of the five dimensions. This decision results in a 1-digit number that expresses the level selected for that dimension. The digits for the five dimensions can be combined into a 5-digit number that describes the patient's health state.

The EQ VAS records the patient's self-rated health on a vertical visual analogue scale, where the endpoints are labelled 'The best health you can imagine' and 'The worst health you can imagine'. The VAS can be used as a quantitative measure of health outcome that reflect the patient's own judgement.

Observed values in the European Quality of Life 5 Dimension 5 Levels (EQ 5D 5L) item responses and VAS scores will be listed only. Dosing regimen will be included in the listing.

11.2.2.2 Short form 36-item (SF-36) domain and composite scores

The SF-36v2, standard recall, measures the following eight health domains as rated by the subjects over the past four weeks: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, and Mental Health. The classification of the questionnaire items to the health domains is shown in Section 13.7.

The SF-36 PCS and MCS scores are used to measure the two broad components, or aspects, of health-physical and mental. PCS and MCS are based on the aggregate of the eight health concepts described above and all of the eight health domain scales are used to score both components summary measures.

One additional item asks responders about health change over the past year.

The SF-36 will be used using QualityMetric's Health Outcomes™ Scoring Software. The software uses updated 2009 U.S. population norms and applies a Full Missing Score Estimation (Full MSE) method as follows:

- A health domain score (except the PF domain) will be estimated provided that at least one non-missing response is available within that domain
- For the PF domain item, response theory will be used to develop a model for estimates of the missing score
- Regression methods are then applied to estimate the PCS and the MCS on the basis of the available domains.

A by-subject listing of the SF-36 item responses will be provided using the SS for all participants by dosing regimen. Dosing regimen will be included in the listing.

11.2.3 Resource Utilization

A listing for the number and length of hospitalizations will be also produced using the ES by dosing regimen.

The number of Infusion Center Admissions will be summarized and listed in a similar manner.

11.2.4 Experience with the Subcutaneous self-administration

PRE-Self Injection Assessment Questionnaire (SIAQ) (Infusion version) domains scores before the first sc self-administration will be listed for participants that self-administer. POST-SIAQ (Infusion version) domains scores will also be listed at each available visit in participants by dosing regimen that self-administer. The SS will be used.

11.3 Specific analyses for Pharmaceuticals and Medical Devices Agency (PMDA)

Separate listings or summaries will not be presented for Japanese participants.

11.4 Headache Questionnaire

The results of the "Symptoms and Frequency of Severe Headache" questionnaire will be listed for each participant. No summary tabulations will be provided for these assessments. The SS will be used.

12 REFERENCES

Levey et al. A New Equation to Estimate Glomerular Filtration Rate. Ann Intern Med. 2009; 150: 604-612.

Nehring, S.M.; Goyal, A.; Patel, B.C. (2020). StatPearls Publishing, web link: https://www.ncbi.nlm.nih.gov/books/NBK441843/.

Rup et al (2015). Clin Exp Immunol. 181:385 – 400.

Shankar et al (2014). AAPS 16:4. DOI:10.1208/s12248-014-9599-2.

United States Department of Health and Human Services, National Cancer Institute. Common Terminology for Adverse Events (CTCAE), Version 5.0, November 17, 2017.

13 APPENDICES

13.1 AE of focus for the Rozanolixizumab Program

The purpose of this appendix is to detail the approach to identifying TEAEs meeting criteria for AEs of focus (AEOF) for the rozanolixizumab program.

Table 13-1: Following Events are Adverse Event of focus For Rozimab for All Indications and for ITP-specific Events:

No	Event (also included in Title of TFL output)	Selection criteria
1	Headache (Note: also included in AESM if severe)	TEAE with HLGT='Headaches'
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)'
3	Hypersensitivity reactions	SMQ='Hypersensitivity'
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 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'
6	Infusion Reactions	Infusion reaction marked on AE CRF page (based on the assessment by the Investigator)
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 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'
10	Effects on the kidney	TEAEs in SMQ= 'Acute renal failure'
11	Drug related hepatic disorders	TEAEs in 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'
13	Thromboembolic events	Embolic and thrombotic events (SMQ)
14	Worsening thrombocytopenia *	Haematopoietic thrombocytopenia (SMQ)
15	Haemorrhagic events *	Haemorrhages (SMQ)

* Data will be summarized by period and listed after adjudication of those events have been properly investigated

13.2 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 CTCAE grade 3 or higher criteria. If both high and low criteria are shown for a parameter, the criteria should be summarized separately in tabular or graphical data summaries.

13.2.1 Hematology

Table 13-2: Hematology Parameters

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 109/L is applied to flag leukocytosis (George 2012).
[2]For ITP protocols, platelets will not be assessed for TEMA because this parameter is expected to be abnormally low due to the participant population and entry criteria.

13.2.2 Chemistry

Table 13-3: Chemistry Parameters

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
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^2	mL/min/1.73 m^2	eGFR <29 mL/min/1.73 m^2
C reactive protein (CRP)[2]	mg/L	mg/L	>10 mg/dL
Corrected Calcium[3]	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
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	mg/dL	mmol/L	<40 mg/dL; <2.2 mmol/L
			High: > 250 mg/dL; >13.9 mmol/L
Total Cholesterol	mg/dL	mmol/L	>400 /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 Common Terminology for Adverse Events (CTCAE), Version 5.0, November 17, 2017 unless otherwise noted.

[1]eGFR is calculated using the Chronic Kidney Disease Epidemiology Collaboration or CKD-EPI formula which is $eGFR = 141 * \min(Scr/\kappa,1)^{\alpha} * \max(Scr/\kappa, 1)^{-1.209} * 0.993^{Age} * 1.018$ [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.

[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/.

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[3]Corrected Calcium is calculated using the formula: Corrected Calcium(mmol/L) =0.02 * (40 – Alb(g/L)) + ca(mmol/L). Note that the normal Albumin level is typically assumed to be equal to 40 g/L.

13.3 Vital sign assessments - abnormal

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

Table 13-4: Vital Sign Parameters

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

13.4 Electrocardiogram (ECG) – Abnormal

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

Table 13-5: ECG Parameters

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

Abbreviations: BL= Baseline, 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 during the Treatment Period (including unscheduled visits) and not meeting the same criteria during Baseline

13.5 ITP-PAQ Scoring

13.5.1 ITP-PAQ Scales

Please see below for the items associated for each scale and the number of points in the Likert Scale that will be used per scale where higher numbers mean better health status.

Table 13-6: ITP Questions

Question	Scale	Response Categories

1	Physical Health: symptoms	0-4
2		
3		
4		
5		
6		
7	Physical Health: fatigue	0-4
8		
9		
10		
11	Physical Health: bother	0-4
12		0-6
13		0-6
14	Physical Health: activity	0-4
15		0-4
16	Emotional Health: psychological	0-4
17		0-4
18		0-4
19		0-4
20		0-4
21	Emotional Health: fear	0-4
22		0-4
23		0-4
24		0-4
25		0-4
26	Overall QoL	0-6
27		0-6
28		0-3
29		0-3
30		0-3
31	Social Activity	0-4
32		0-4
33		0-4
34		0-4
35	Women's reproductive health	0-4
36		0-4
37		0-4
38		0-4
39		0-4
40		0-4
41	Work	0-5
42		0-5
43		0-5
44		0-5

The ITP-PAQ domain scores will be obtained by transforming the raw sum of the item responses to a 0-100 scale. This can be obtained using the following formula:

$$\text{ITP-PAQ score} = \frac{\text{Sum of item scores within the scale}}{\text{raw sum range}} * 100$$

ITP-PAQ domain	Raw sum range
Symptoms	24
Fatigue	16

Bother	16
Activity	8
Psychological health	20
Fear	20
Work	20
Social activity	16
Women's reproductive health	24
Overall Quality of Life	21

Missing data:

A domain score is not calculated if more than half of the items of this domain are missing.

If 50% or more of the items are available, missing items are imputed using the mean of non-missing items. For domains that include items with a different number of categories, the imputed response for missing items has to be transformed on the range of the response scale of the missing item.

13.6 ITP bleeding score

The ITP-BAT tool version 1.0 consists of the following domains:

- Skin (S)
- Visible mucosae (M)
- Organs (O)

The domain for skin comprises the following bleeding types:

- Petechiae
- Ecchymoses
- Subcutaneous hematomas
- Bleeding from minor wounds

The domain for visible mucosae comprises the following bleeding types:

- Epistaxis
- Oral cavity- gum bleeding
- Oral cavity – hemorrhagic bullae or blisters
- Oral cavity – bleeding from bites to lips and tongue or after deciduous teeth loss
- Subconjunctival hemorrhage (not due to conjunctival disease)

The domain for organs comprises the following bleeding types:

- Gastrointestinal bleeding not explained by visible mucosal bleeding or lesion
- Lung bleeding
- Hematuria

- Menorrhagia
- Intramuscular hematomas
- Hemarthrosis
- Ocular bleeding
- Intracranial bleeding
- Other internal bleeding

The grading for each bleeding type within each domain is presented in Table 13-7. Each bleeding type is graded based on the worst manifestation that occurred during the most recent observation period (since the previous visit). The grade for each domain is then taken as the worst (most severe) grade across all bleeding types within that domain.

Missing data will not be imputed. In the case that data for one or more bleeding types are missing within a given domain, the grade for that domain will be evaluated based on the available data. In the case that no data are available within a given domain, the score for that domain will not be evaluated at the specific visit.

Table 13-7: ITP-BAT scoring

Type of bleeding	**GRADES BASED ON THE WORST INCIDENT EPISODE SINCE LAST VISIT[2]**				
	0	**1**	**2**	**3**	**4**
SKIN					
Petechiae (does not include steroid–induced or senile purpura)	☐ No	☐ Less than or equal to 10 in a patient's palm-sized area[3] in the most affected body area[4]	☐ More than 10 in a patient's palm-sized area or more than 5 in at least 2 patient's palm-sized areas located in at least 2 different body areas[4], one above and one below the belt (in the most affected body areas) [4]	☐ More than 50, if scattered both above and below the belt	
Ecchymoses	☐ None or up to 2 in the same body area[4], but	☐ 3 or more in the same body area[4], but all smaller	☐ From 1 to 5 larger than a patient's palm-sized	☐ More than 5 larger than a patient's	

Type of bleeding	GRADES BASED ON THE WORST INCIDENT EPISODE SINCE LAST VISIT[2]				
	0	**1**	**2**	**3**	**4**
	smaller than a patient's palm-sized area, if a) spontaneous **or** b) disproportionate to trauma/constriction[5]	than a patient's palm-sized area, if a) spontaneous **or** b) disproportionate to trauma/constriction[5] ☐ At least 2 in two different body areas[4], smaller than a patient's palm-sized area, if a) spontaneous **or** b) disproportionate to trauma/constriction[5] ☐ Any number and size if reported by the patient	area, if a) spontaneous **or** b) disproportionate to trauma/constriction[5] with or without smaller ones	palm-sized area, if a) spontaneous **or** b) disproportionate to trauma/ constriction[5]	
Subcutaneous hematomas	☐ No	☐ 1 smaller than a patient's palm-sized area ☐ Any number and size if	☐ 2 smaller than a patient's palm-sized area, spontaneous ☐ 2 smaller than a patient's palm-sized	☐ More than 2 smaller or at least 1 larger than a patient's palm-sized	

Type of bleeding	GRADES BASED ON THE WORST INCIDENT EPISODE SINCE LAST VISIT[2]				
	0	**1**	**2**	**3**	**4**
		reported by the patient	area, disproportionate to trauma[5]	area, spontaneous ☐ More than 2 smaller or at least 1 larger than a patient's palm-sized area, disproportionate to trauma[5]	
Bleeding from minor wounds[6]	☐ No	☐ Lasting <=5 min ☐ Any episode if reported by the patient	☐ Lasting >5 min or interfering with daily activities	☐ Requiring protracted medical observation at the time of this visit ☐ Medical report describing patient's evaluation by a physician	
MUCOSAL					
Epistaxis[7]	☐ No	☐ Lasting <=5 min ☐ Any episode if reported by the patient	☐ Lasting >5 min or interfering with daily activities	☐ Packing or cauterization or in-hospital evaluation at the time of this visit ☐ Medical report describing packing or	☐ RBC transfusion or Hb drop >2g/dL

Type of bleeding	GRADES BASED ON THE WORST INCIDENT EPISODE SINCE LAST VISIT[2]				
	0	**1**	**2**	**3**	**4**
				cauterization or in-hospital evaluation	
Oral cavity – gum bleeding[7]	☐ No	☐ Lasting <=5 min ☐ Any episode if reported by the patient	☐ Lasting >5 min or interfering with daily activities	☐ Requiring protracted medical observation at the time of this visit ☐ Medical report describing patient's evaluation by a physician	
Oral cavity – hemorrhagic bullae or blisters	☐ No	☐ Less than 3 ☐ Any number if reported by the patient	☐ From 3 to 10 but no difficulty with mastication	☐ More than 10 or more than 5 if difficulty with mastication	
Oral cavity - bleeding from bites to lips & tongue or after deciduous teeth loss	☐ No	☐ Lasting <=5 min ☐ Any episode if reported by the patient	☐ Lasting >5 min or interfering with daily activities	☐ Interventions to ensure hemostasis or in-hospital evaluation at the time of this visit ☐ Medical report describing interventions to ensure hemostasis	

Type of bleeding	GRADES BASED ON THE WORST INCIDENT EPISODE SINCE LAST VISIT[2]				
	0	**1**	**2**	**3**	**4**
				or in-hospital evaluation	
Subconjunctival hemorrhage (not due to conjunctival disease)	☐ No	☐ Petechiae/ hemorrhage partially involving one eye ☐ Any episode if reported by the patient	☐ Petechiae/ hemorrhage partially involving both eyes, or diffuse hemorrhage in one eye	☐ Diffuse hemorrhage in both eyes	
ORGAN (and internal mucosae)					
Gastrointestinal bleeding not explained by visible mucosal bleeding or lesion: Hematemesis, Melena, Hematochezia, Rectorrhagia	☐ No	☐ Any episode if reported by the patient	☐ Present at the visit ☐ Described in a medical report	☐ Requiring endoscopy[8] or other therapeutic procedures or in-hospital evaluation at the time of this visit ☐ Medical report prescribing endoscopy[8] or other therapeutic procedures or in-hospital evaluation	☐ RBC transfusion or Hb drop >2g/dL

Type of bleeding	GRADES BASED ON THE WORST INCIDENT EPISODE SINCE LAST VISIT[2]				
	0	**1**	**2**	**3**	**4**
Lung bleeding Hemoptysis Tracheobronchial bleeding	☐ No	☐ Any episode if reported by the patient	☐ Present at this visit ☐ Described in a medical report	☐ Requiring bronchoscopy[8] or other therapeutic procedures or in-hospital evaluation at the time of this visit ☐ An equivalent episode if described in a medical report	☐ RBC transfusion or Hb drop >2g/dL
Hematuria	☐ No	☐ Any episode if reported by the patient ☐ Microscopic (lab analysis exhibited)	☐ Macroscopic (lab analysis exhibited) ☐ Described in a medical report	☐ Macroscopic, and requiring cystoscopy[8] or other therapeutic procedures or in-hospital evaluation at the time of this visit ☐ An equivalent episode if described in a medical report	☐ RBC transfusion or Hb drop >2g/dL
Menorrhagia (compared to pre-ITP or to	☐ No	☐ Doubling nr. of pads or tampons in last cycle	☐ Changing pads more frequently than every 2 hrs. or	☐ Acute menorrhagia requiring hospital	☐ RBC transfusion

Type of bleeding	GRADES BASED ON THE WORST INCIDENT EPISODE SINCE LAST VISIT[2]				
	0	**1**	**2**	**3**	**4**
a phase of disease with normal platelet count)[9]		compared to pre-ITP or to a phase of disease with normal platelet count ☐ Score >100 using PBAC in the last cycle, if normal score in pre-ITP cycles or in a phase of disease with normal platelet count	clot and flooding ☐ Requiring combined treatment with antifibrinolytics and hormonal therapy or gynecological investigation (either at this visit or described in a medical report)	admission or endometrial ablation (either at this visit or described in a medical report)	or Hb drop >2g/dL
Intramuscular hematomas (only if diagnosed by a physician with an objective method)	☐ No	☐ Post trauma, diagnosed at this visit, if judged disproportionate to trauma ☐ An equivalent episode if described in a medical report	☐ Spontaneous, diagnosed at this visit ☐ An equivalent episode if described in a medical report	☐ Spontaneous or post trauma (if judged disproportionate to trauma) diagnosed at this visit and requiring hospital admission or surgical intervention ☐ An equivalent episode if described in a medical report	☐ RBC transfusion or Hb drop >2g/dL
Hemarthrosis	☐ No	☐ Post trauma,	☐ Spontaneous,	☐ Spontaneou	☐ Spontaneou

Type of bleeding	GRADES BASED ON THE WORST INCIDENT EPISODE SINCE LAST VISIT[2]				
	0	**1**	**2**	**3**	**4**
(only if diagnosed by a physician with an objective method)		diagnosed at this visit, function conserved or minimally impaired, if judged disproportionate to trauma ☐ An equivalent episode if described in a medical report	diagnosed at this visit, function conserved or minimally impaired ☐ An equivalent episode if described in a medical report	s or post trauma (if judged disproportionate to trauma), diagnosed at this visit and requiring immobilization or joint aspiration ☐ An equivalent episode if described in a medical report	s or post trauma (if judged disproportionate to trauma) diagnosed at this visit and requiring surgical intervention ☐ An equivalent episode if described in a medical report
Ocular bleeding (only if diagnosed by a physician with an objective method)	☐ No		☐ Any post trauma vitreous or retinal hemorrhage involving one or both eyes with or without impaired/blurred vision present at this visit if judged disproportionate to trauma ☐ An equivalent episode if described in a medical report	☐ Spontaneous vitreous or retinal hemorrhage involving one or both eyes with impaired/blurred vision present at this visit ☐ An equivalent episode if described in a medical report	☐ Spontaneous vitreous or retinal hemorrhage with loss of vision in one or both eyes present at this visit ☐ An equivalent episode if described in a medical report
Intracranial bleeding[10]:	☐ No		☐ Any post trauma event	☐ Any spontaneous event	☐ Any spontaneous event

Type of bleeding	GRADES BASED ON THE WORST INCIDENT EPISODE SINCE LAST VISIT[2]				
	0	**1**	**2**	**3**	**4**
intracerebral, intraventricular, subarachnoidal, subdural, extradural **(only if diagnosed with an objective method at the visit or described in a medical report provided by the patient)**			requiring hospitalization	requiring hospitalization in presence of an underlying intracranial lesion	requiring hospitalization without an underlying intracranial lesion
Other internal bleeding: hemoperitoneum hemopericardium hemothorax retroperitoneal bleeding hepatic and splenic peliosis with organ rupture retroorbital bleeding metrorrhagia etc. **(only if diagnosed with an objective method at the**	☐ No			☐ Any event requiring hospitalization <48 hrs.	☐ Any event requiring hospitalization >48 hrs. or RBC transfusion or Hb drop >2g/dL

Type of bleeding	GRADES BASED ON THE WORST INCIDENT EPISODE SINCE LAST VISIT[2]				
	0	1	2	3	4
visit or described in a medical report provided by the patient)					

Grading is based on physical examination at the time of the visit by the physician or expert nurse or on patient's history supplemented by available medical reports. Bleeding manifestations reported by the patient but not visible at the time of data collection are graded 1. Grade 5 is assigned to fatal bleeding.
To receive a grade >1, all non-overt skin and non-overt mucosal bleeding (petechiae, ecchymoses, subcutaneous hematomas, vesicles/bullae subconjunctival bleeding) should be visible at the time of visit for grading by the physician or expert nurse taking the history.
For bleeding from minor wounds and overt-mucosal bleeding (epistaxis, gum, bleeding from bites to lips & tongue or after deciduous teeth loss/extraction) and all organ bleeding, a medical record describing the symptom or indicating a specific intervention/prescription should be also taken into account for grading.
Requirement for ITP-specific treatments and anti-fibrinolytics (apart from menorrhagia) was not considered for grading, due to their subjective nature and their adoption not only to control actual bleeding but also to reduce the "risk" of impendent or future bleeding.

[1] In case of patients examined for the first time, all types of bleeding occurring at the visit and in the 15 days preceding the visit should be considered.
[2] Each type of bleeding should be graded based on the worst bleeding manifestation that occurred during each observation period or in the 15 days preceding the first visit.
[3] Patient's own palm size is commonly considered to be proportional to body surface area. Palm = the inner surface of the hand stretching between the distal crease of the wrist and the bases of the fingers (fingers surface excluded).
[4] Body areas include: face, neck, right and left upper limbs (considered separately), right and left lower limbs (considered separately), trunk, abdomen, and recumbent areas (for the ambulatory patient means the area below the knees).
[5] Bleedings considered proportionate to trauma/constriction on a clinical ground should not be reported for skin domain.
[6] Minor wound means superficial skin cuts (eg, by shaving razor, knife, or scissors).
[7] Epistaxis and gum bleeding are also reported in some normal subjects. Thus, a critical judgment is required in grading these manifestations; they should be reported only if judged more severe when compared with pre-ITP bleeding, if any.
[8] Any endoscopic investigations should be considered for grading only if performed for therapeutic purpose and not solely for diagnostic purpose.
[9] In girls at menarche grade 1 cannot be assigned, lacking comparison with previous cycles.
[10] Intracranial bleeding should always be reported, irrespective of its grade. For example, if a woman had S2 (subcutaneous hematoma) M2 (epistaxis) O3 (menorrhagia) and an intracranial bleeding grade 2 (post trauma, requiring hospitalization), the SMOG index is S2M2O3 (intracranial 2). If the same patient also had intracranial bleeding grade 3, the SMOG index is S2M2O3 (intracranial 3).

13.7 Classification of the SF-36v2 questionnaire

Table 13-8: SF-36V2 Questions

[redacted]	**Scales**
	Physical Functioning
	Role-Physical
	Bodily Pain
	General Health
	Vitality
	Social Functioning
	Role-Emotional
	Mental Health

14 AMENDMENT(S) TO THE STATISTICAL ANALYSIS PLAN (SAP)

14.1 AMENDMENT 1

Rationale for the amendment

The primary reason for this SAP amendment is to incorporate the changes from Protocol Amendment 4 and the reduced scope of analyses following sponsor's decision to terminate the study early.

Table 14-1: Modifications and changes

Section # and Name	Description of Change	Brief Rationale
2.1.3	Removed objective "To evaluate the effects of rozanolixizumab on exploratory biomarkers"	Updated to align with Protocol Amendment 4
2.1.3	Added objective "To assess the effect of rozanolixizumab on response to vaccination in study participants who received COVID-19 vaccine"	
2.2.2.4	Removed "Including all intermediate timepoints" from ITP-PAQ endpoint	
2.2.3.4	Changed text of IgG, IgA, IgE and IgM endpoints	
2.2.3.5	Removed ITP-specific autoantibodies endpoint	
2.2.3.7	Removed several exploratory endpoints	
2.2.3.7	Added COVID-19 vaccination endpoint	
2.2.1.2	Removed α-globulin, and β-globulin endpoints	
2.2.1.2	Removed Cytokines endpoint	
2.3	Removed the exploratory arm	
2.3	Dosing is [redacted] instead of [redacted]	
2.3	Various other changes to study design that do not have a direct impact on analysis	
3.2.4	Definition of dosing regimen groups ([redacted] and [redacted]	Need to define subsets of protocol-defined analysis sets which will be used for analysis
3.5.4	Change complete infusion to sufficient infusion	Requested by FDA
3.7	Updated to MedDRA version 24 dictionary	New version available

Section # and Name	Description of Change	Brief Rationale
3.7	Updated to WHODD, Mar 2021 version	New version available
3.8	Text added to describe analysis omitted because of early termination of study.	Sponsor decision to terminate study early.
4.1	Text referring to sensitivity analysis and MI MAR analysis removed.	Analysis no longer required.
4.1.3	Changed intercurrent event strategy for COVID-19 to composite strategy and platelet data set to 0	Requested by FDA
6.5.1	Modification to assignment of medications to treatment period	Be consistent with the definition of treatment period
9.1.1	Analysis has been removed.	Owing to the sponsor's decision to terminate this study the analysis is no longer required.
9.2.2 – 9.2.4, 9.2.6 – 9.2.7	Analysis has been removed.	
9.3	Analysis has been removed.	
9.4	Analysis has been removed.	
9.2.1	All formal statistical analysis has been removed	
11.2.1	Text modified to reflect that item responses will be listed only, no derived scores will be calculated, and no change from baseline will be computed.	
11.2.2	Text added to reflect that item responses will be listed only, no derived scores will be calculated, and no change from baseline will be computed.	
10.2	Updated the analysis for antidrug antibodies	Owing to the sponsor's decision to terminate this study the majority of the analysis is no longer required.
10.3.1 – 10.3.3	Changed text of IgG, IgA, IgE and IgM endpoints	Updated to align with Protocol Amendment 4
10.3.2, 10.4.3	Removed ITP-specific autoantibodies endpoint	
10.5	Removed several exploratory endpoints	
8.6	Clarified definition for time at risk	Align with TP0003/6 definition

Section # and Name	Description of Change	Brief Rationale
8.2	Clarified definitions of severity and intensity for adverse events	Clarify how severe adverse events will be summarized
8.2.2	Add AESIs and TEAEs leading to study discontinuation to overview	Categories in overview should match categories in adverse event tables
8.2.2	Removed some adverse event tables	No longer needed
8.2.2	Added AEs of focus: hemorrhagic events, worsening thrombocytopenia and effect on lipids	These were added to the AE of Focus document 3.0, or they were removed from the document but were still considered relevant for ITP
8.5.1	Added "All values must be met at the same sample taken from the same visit"	Clarified how PDILI is defined
8.5.1	Added the components of the Hy's law definition presented separately in a stepwise fashion to the table	Provide more information about the components of PDILI
8.7	Removed α-globulin, and β-globulin endpoints	Updated to align with Protocol Amendment 3
8.8	Removed change from baseline for Complement endpoint	Owing to the sponsor's decision to terminate this study the analysis is no longer required.
8.9	Removed Cytokines endpoint	Updated to align with Protocol Amendment 3
Throughout	Minor editorial and formatting changes have been made.	Minor, therefore have not been summarized.

STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

This document has been reviewed and approved per the Review and Approval of Clinical Documents Standard Operating Procedures. Signatures indicate that the final version of the Statistical Analysis Plan (SAP) or amended SAP is released for execution.

Approval Signatures

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