TRIAL STATISTICAL ANALYSIS PLAN

Document No.:	**c43536758-01**
BI Trial No.:	**1434-0016**
Title:	A phase I, open-label, two-arm, non-randomised trial to investigate the metabolism and pharmacokinetics of a single dose of BI 764198 (C-14) administered as oral solution using two different approaches in healthy male volunteers Final revised protocol (Version 3.0, 10 Aug 2023, c38438177-03)
Investigational Product(s):	BI 764198
Responsible trial statistician(s):	[redacted] on behalf of: [redacted]
Date of statistical analysis plan:	08 Dec 2023
Version:	1.0

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2. LIST OF ABBREVIATIONS

See Medicine Glossary:
http://glossary

Term	Definition / description
ADME	Absorption, distribution, metabolism, and excretion
AE	Adverse event
[redacted]	
AESI	Adverse events of special interest
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
[redacted]	
$AUC_{0\text{-}24hr}$	Area under the concentration-time curve of the analyte in plasma over the
[redacted]	
BI	Boehringer Ingelheim
BP	Blood pressure
[redacted]	
CL	Total clearance of the analyte in plasma after intravascular administration
[redacted]	
COVID-19	Corona virus disease 2019
CRF	Case Report Form, paper or electronic (sometimes referred to as ‘eCRF’)

Term	Definition / description
CTP	Clinical trial protocol
CTR	Clinical trial report
DILI	Drug induced liver injury
DMC	Data monitoring committee
ECG	Electrocardiogram
eCRF	Electronic case report form
eDC	Electronic data capture
eDMS	Electronic Document Management System
EoS	End of Study (synonym for End of Trial)
EudraCT	European Clinical Trials Database
F	Absolute bioavailability factor
$fe_{faeces,0\text{-}tz}$	fraction of [^{14}C]-radioactivity excreted in faeces expressed as percentage of the administered dose over the time interval from 0 to the last quantifiable time point
$fe_{urine,0\text{-}tz}$	Fraction of [^{14}C]-radioactivity excreted in urine expressed as percentage of the administered dose over the time interval from 0 to the last quantifiable time point
[redacted]	
FU	Follow-up
GCP	Good Clinical Practice
gMean	Geometric mean
[redacted]	
IB	Investigator's brochure
IPD	Important protocol deviation
[redacted]	
MedDRA	Medical Dictionary for Regulatory Activities
[redacted]	
PKS	Pharmacokinetic parameter analysis set

Term	Definition / description
PR	Pulse rate
QT interval	ECG interval from the start of the QRS complex to the end of the T wave
QTc interval	QT interval corrected for heart rate, e.g. using the method of Fridericia (QTcF) or Bazett (QTcB)
[redacted]	
SAE	Serious adverse event
SCR	Screening
SOP	Standard operating procedure
[redacted]	
TS	Treated set
t_z	Time of last measurable concentration of the analyte in plasma
TSAP	Trial statistical analysis plan
ULN	Upper limit of normal
[redacted]	

3. INTRODUCTION

As per ICH E9 (1) the purpose of this document is to provide a more technical and detailed elaboration of the principal features of the analysis described in the protocol, and to include detailed procedures for executing the statistical analysis of the primary and secondary variables and other data.

This TSAP assumes familiarity with the Clinical Trial Protocol (CTP), including Protocol Amendments. In particular, the TSAP is based on the planned analysis specification as written in CTP Section 7 “Statistical Methods and Determination of Sample Size”. Therefore, TSAP readers may consult the CTP for more background information on the study, e.g., on study objectives, study design and population, treatments, definition of measurements and variables, planning of sample size, randomization and the changes implemented in V3 of the CTP.

Study data as collected in the eCRF will be stored in a trial database within the RAVE EDC system. All study data also including external data will then be uploaded to the CDR data warehouse.

The statistical analyses will be performed within the validated working environment CARE, including SAS™ (current Version 9.4, by [redacted]), and a number of SAS™-based tools (e.g., macros for the analyses of AE data or laboratory data; Report Appendix Generator system (RAGe) for compilation/formatting of the CTR appendices).

PK parameters will be calculated using Phoenix WinNonlin™ software (version Phoenix 8.1, [redacted]).

4. CHANGES IN THE PLANNED ANALYSIS OF THE STUDY

All analyses described in this TSAP are in accordance with the statistical methods described in the CTP.

5. ENDPOINTS(S)

Subjects in cohort 2b received the same treatment, using the same approach as for subjects in cohort 2a. However, for subjects in cohort 2b fewer endpoints are determined compared with cohort 2a, see Table 7.2.1 of CTP.

Table 5: 1 Overview of endpoints analysed per cohort

Endpoint	Cohort 1	Cohort 2a	Cohort 2b
Primary endpoint	X	X	
Secondary endpoints	X	X	X
Further endpoint regarding			
Pharmacokinetic	X	X	X*
Safety	X	X	X

* Further PK endpoints for cohort 2b will be calculated as appropriate based on the available assessments.

CTP: In general, the descriptive analysis will be done by cohort: cohort 1, cohort 2a, cohort 2b and in addition for a general assessment of the microtracer approach, based on pooled data from cohorts 2a and 2b.

5.1 PRIMARY ENDPOINT(S)

Primary endpoints are as defined in Section 2.1.2 of the **CTP**:

The following pharmacokinetic parameters will be determined for BI 764198 for each respective approach (classical hADME and microtracer hADME):

Mass balance recoveries of total radioactivity in urine and faeces:

- $fe_{urine,0\text{-}tz}$ *(fraction of [^{14}C]-radioactivity excreted in urine expressed as percentage of the administered dose over the time interval from 0 to the last quantifiable time point)*
- $fe_{faeces,0\text{-}tz}$ *(fraction of [^{14}C]-radioactivity excreted in faeces expressed as percentage of the administered dose over the time interval from 0 to the last quantifiable time point)*

CTP: *To avoid underestimation of the total recovery of [^{14}C] in subjects who do not meet release criteria on Day 10, the excretion during the non-sampling phase of the study will be estimated using linear interpolation between the observed 24-h sampling periods before and after the non-sampling period for urine and faeces.*

5.2 SECONDARY ENDPOINT(S)

5.2.1 Key secondary endpoint(s)

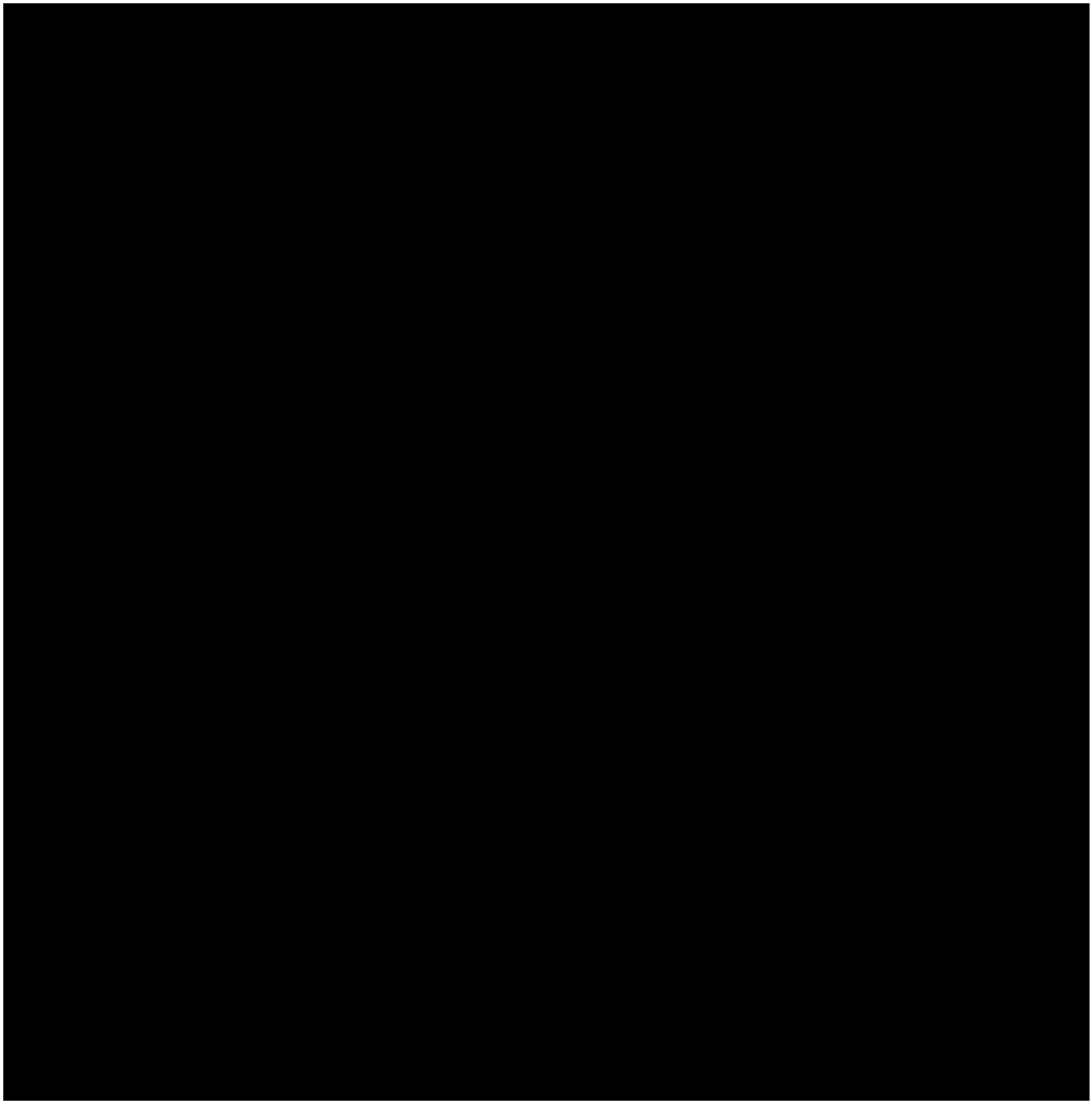
Not applicable.

5.2.2 Secondary endpoint(s)

Secondary endpoints are PK endpoints of [^{14}C]-radioactivity and BI 764198 in plasma, as defined in section 2.1.3 of the **CTP**:

- *C_{max} (maximum measured concentration of the analyte) in plasma*
- *$AUC_{0\text{-}tz}$ (area under the concentration-time curve of the analyte over the time interval from 0 to the last quantifiable data point) in plasma*

[redacted]



5.3.2 Safety parameters

Safety and tolerability of BI 764198 will be assessed based on further safety parameters defined in Section 2.2.2.2 of the **CTP**:

- *Adverse events (including clinically relevant findings from the physical examination)*
- *Safety laboratory tests*
- *12-lead ECG*
- *Vital signs (blood pressure, pulse rate)*

5.4 OTHER VARIABLE(S)

5.4.1 Demographic and other baseline characteristics

CTP: *At screening, the medical examination will include demographics, height and body weight, smoking and alcohol history (alcohol history not mandatory to be entered into CRF or to be reported), relevant medical history and concomitant therapy, review of inclusion and exclusion criteria, review of vital signs (BP, PR), 12-lead ECG, laboratory tests, and a physical examination. At the end-of-study examination, medical examination will include the review of vital signs, 12-lead ECG, laboratory tests, and a physical examination including body weight.*

Body mass index will be calculated as weight [kg] / height $[m]^2$.

5.4.2 Treatment compliance and treatment exposure

Treatment compliance will not be analysed as a specific endpoint, cf. Section 4.3 of the CTP.

Since only single doses will be applied, the date, time of administration will be sufficient to give account of treatment exposure.

6. GENERAL ANALYSIS DEFINITIONS

6.1 TREATMENT(S)

For basic study information on the treatment to be administered, and selection of dose, cf. Section 4 of the CTP.

There are two study arms. In both study arms a single dose of [redacted]BI 764198 is used. The most notable difference between Arm 1 and 2 is that Arm 1 uses a traditional [redacted]-labelled tracing, while Arm 2 employs a [redacted]-labelled microtracer approach with much lower radioactive dose. The radioactive compound and associated radioactivity differs as described in Table 1.4.2:1 and Appendix 10.1 in **CTP**.

With CTP version 3.0 an additional cohort assessing the microtracer approach was introduced as due to processing errors no reliable metabolite profiling was possible for the first 8 subjects receiving the microtracer approach. Thus, study arm 2 consists of 2 cohorts: cohort 2a and cohort 2b.

For statistical analysis of AEs, the following analysis phases are defined for each subject.

Table 6.1: 1 Analysis phases for statistical analysis of AEs, and actual treatment for analysis of laboratory data and vital signs

Study analysis phase	**Label**	**Start**	**End**
Screening	**Screening**	Date of informed consent	Date/time of administration of study drug
On treatment	**Cohort 1, Cohort 2a, Cohort 2b***	Date/time of administration of study drug	Date/time of administration of study drug + [redacted] or 12:00 a.m. on day after last contact date (whichever occurs first)
Follow-up	**F/U**	Date/time of administration of study drug + [redacted]	12:00 a.m. on day after last contact date

*depending on the assigned cohort

The following AE displays will be provided in the report:

- Section 15.3 and Appendix 16.1.13.1.8 (for ClinicalTrials.gov and EudraCT only) of the CTR displays

In these displays, the on-treatment phase will be analysed (labelled with the name of the cohort). Screening and follow-up periods will not be included in this analysis.

The following total will be provided in addition (Section 15.3 only):

  - "Total cohort 2", defined as the total over all on-treatment phases involving BI administered using the microtracer approach

- Section 15.4 of the CTR displays:
  - Screening
  - On-treatment (labelled with the name of the cohort)

All AEs will be listed.

Safety laboratory data, vital signs and PK parameters will be analysed (based on cohorts) with clear differentiation between baseline and on-treatment measurements. Measurements will be considered on-treatment, if they were taken within the on-treatment phase as defined in Table 6.1: 1.

More details on the technical implementation of these analyses are provided in the ADS Plan of this TSAP.

6.2 IMPORTANT PROTOCOL DEVIATIONS

Consistency check listings (for identification of deviations from time windows) and a list of protocol deviations (e.g. deviations in drug administration, in blood sampling times, etc.) will be provided for discussion at the Report Planning Meeting. At this meeting, it will be decided whether a discrepant data value can be used in analyses or whether it must be corrected in the clinical database. Each protocol deviation must be assessed to determine whether it is an important PD (iPD). For definition of iPDs, and for the process of identification of these, refer to the BI reference document "Identify and Manage Important Protocol Deviations (iPD)" (2) and the DV domain template.

If any iPDs are identified, they are to be summarised into categories and will be captured in the decision log. Categories which are considered to be iPDs in this trial are defined in the DV domain template. If the data show other iPDs, the definition in the DV domain template will be supplemented accordingly by the time of the Report Planning Meeting.

iPDs will be summarised and listed. Which kind of iPDs could potentially lead to exclusion from which analysis set is specified in the DV domain template. The decision on exclusion of subjects from analysis sets will be made at the latest at the Report Planning Meeting, after discussion of exceptional cases and implications for analyses.

Non-important COVID-19 related PDs will be summarised and listed.

Handling of iPDs in analysis is included in the DV domain specifications and stored within the TMF in EDMS.

6.3 INTERCURRENT EVENTS

This section is not applicable.

6.4 SUBJECT SETS ANALYSED

Subject sets will be used as defined in the CTP, Section 7.

- *Treated set (TS): The treated set includes all subjects who were treated with at least one dose of trial drug. The treated set will be used for safety analyses.*

- *Pharmacokinetic parameter analysis set (PKS): This set includes all subjects in the treated set (TS) who provide at least one PK endpoint that was defined as primary or secondary and was not excluded due to a protocol deviation relevant to the evaluation of PK or due to PK non-evaluability* (as defined in section 7.2.1.2 of CTP)*. Thus, a subject will be included in the PKS, even if he contributes only one PK parameter value for one period to the statistical assessment. Descriptive analyses of PK parameters will be based on the PKS.*

Table 6.4: 1 Subject sets analysed

	Subject set	
Class of endpoint	Treated set	PKS
Primary endpoint		X
Secondary and further PK endpoints		X
Further safety endpoints & treatment exposure	X	
Disposition	X	
iPDs	X	
Demographic/baseline endpoints	X	

[redacted]

6.6 HANDLING OF MISSING DATA AND OUTLIERS

6.6.1 Safety

CTP: *It is not planned to impute missing values for safety parameters.*

One exception where imputation might be necessary for safety evaluation is AE dates. Missing or incomplete AE dates are imputed according to BI standards (3).

6.6.2 Pharmacokinetics

CTP: *Handling of missing PK data will be performed according to the relevant BI internal procedures (4).*

PK parameters that cannot be reasonably calculated based on the available drug concentration-time data will not be imputed.

6.7 BASELINE, TIME WINDOWS AND CALCULATED VISITS

The last available value determined prior to study drug administration will be defined as baseline.

Time windows are defined in Section 6.1 of the CTP. Adherence to time windows will be checked at the Report Planning Meeting.

7. PLANNED ANALYSIS

The format of the listings and tables will follow the BI guideline "Reporting of clinical trials and project summaries" (5).

The individual values of all subjects will be listed. Listings will be sorted by cohort, subject number and visit (if visit is applicable in the respective listing). AE listings will be sorted by assigned treatment (cohort) (see Section 7.8.1 for details). The listings will be contained in Appendix 16.2 (SDL) of the CTR.

The following standard descriptive statistical parameters will be displayed in summary tables of continuous variables:

N	number of non-missing observations
Mean	arithmetic mean
SD	standard deviation
Min	minimum
Median	median
Max	maximum

For serum concentrations as well as for all PK parameters the following descriptive statistics will additionally be calculated:

CV	arithmetic coefficient of variation
gMean	geometric mean
gCV	geometric coefficient of variation

For PK parameters the following descriptive statistics will additionally be calculated:

P10	10th percentile
Q1	1st quartile
Q3	3rd quartile
P90	90th percentile

CTP: *In general, the descriptive analysis will be done by cohort: cohort 1, cohort 2a, cohort 2b and in addition for a general assessment of the microtracer approach, based on pooled data from cohorts 2a and 2b.*

The data format for descriptive statistics of serum concentrations will be identical with the data format of the respective concentrations. The descriptive statistics of PK parameters will be calculated using the individual values with the number of decimal places as provided by the evaluation program. Then the individual values as well as the descriptive statistics will be reported with three significant digits in the CTR.

Tabulations of frequencies for categorical data will include all possible categories and will display the number of observations in a category as well as the percentage (%) relative to the respective treatment group. Percentages will be rounded to one decimal place. The category missing will be displayed if and only if there actually are missing values. Percentages will be

based on all subjects in the respective subject set whether they have non-missing values or not.

7.1 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Only descriptive statistics are planned for this section of the report.

7.2 CONCOMITANT DISEASES AND MEDICATION

Only descriptive statistics are planned for this section of the report.

Concomitant diseases and non-drug therapies will be coded according to the most recent version of the coding system of the Medical Dictionary for Drug Regulatory Activities (MedDRA). Concomitant medication will be coded according to the most recent version of the World Health Organization - Drug Dictionary (WHO-DD). The coding version number will be displayed as a footnote in the respective output.

CTP: *Previous and concomitant therapies will be presented per treatment group without consideration of time intervals and treatment periods.*

A medication will be considered concomitant to a treatment, if it

- is ongoing at the time of study drug administration, or
- starts within the analysis phase of the respective treatment (see Section 6.1 for a definition of treatments and analysis phases).

The relevance of the concomitant therapies to the evaluation of PK will be decided no later than at the RPM.

7.3 TREATMENT COMPLIANCE

Treatment compliance will not be analysed as a specific endpoint. Any deviations from complete intake will be addressed in the RPM (cf. Section 6.2) and described in the CTR.

7.4 PRIMARY OBJECTIVE ANALYSIS

Independent of the main objectives stated in the CTP, this section describes further details of the primary endpoint analyses outlined in the CTP.

7.4.1 Main analysis

Only descriptive statistics are planned for this section of the CTR. These will be based on the PKS.

Exclusion of PK parameters:

The ADS ADPP (PK parameter per time-point or per time-interval) contains column variables APEX and APEXCO indicating inclusion/exclusion (APEX) of a PK parameter and an

analysis flag comment (APEXCO). All analyses based on the PKS are based on PK parameter values which are not flagged for exclusion, i.e. with APEX equal to "Included".

CTP: *Plasma, urine, faeces and if applicable vomiting concentration data and parameters of a subject which are flagged for exclusion will be reported with its individual values but will not be included in the descriptive statistics.*

Exclusion of PK concentrations:

The ADS ADPC (PK concentrations per time-point or per time-interval) contains column variables ACEX or ACEXCO indicating inclusion/exclusion (ACEX) of a concentration and an analysis flag comment (ACEXCO). Exclusion of a concentration depends on the analysis flag comment ACEXCO. For example, if ACEXCO is set to "ALL CALC", the value will be excluded for all types of analyses based on concentrations. If ACEXCO is set to "DESC STATS" the value will be excluded from descriptive evaluations per planned time point/time interval. If ACEXCO contains the addition "TIME VIOLATION" or "TIME DEVIATION", the value can be used for further analyses based on actual times. If ACEXCO is set to "HALF LIFE", the value will be excluded from half-life calculation only; the value is included for all other analyses. Excluded concentration itself will be listed in the CTR associated with an appropriate flag.

Further details are given in "Noncompartmental Pharmacokinetic / Pharmacodynamic Analyses of Clinical Studies"(4) and "Description of Analytical Transfer Files and PK/PD Data Files" (9).

7.4.4 Supplementary analysis

This section is not applicable as no supplementary analysis have been specified in the protocol.

7.5 SECONDARY OBJECTIVE ANALYSIS

Independent of the main objectives stated in the CTP, this section describes further details of the second endpoint analyses.

7.5.1 Key secondary objective analysis

This section is not applicable as no key secondary endpoint has been specified in the protocol.

7.5.1.1 Main analysis

Not applicable (see 7.5.1).

[redacted]

7.5.1.4 Supplementary analysis

Not applicable (see 7.5.1).

7.5.2 Secondary objective analysis

The analysis of secondary PK endpoints will be based on the PKS.

CTP: *The secondary endpoints (refer to Section 2.1.3) will be calculated according to the relevant BI internal procedures and will be assessed statistically using the same methods as described for the primary endpoints.*

Exclusion of PK parameters and exclusion of plasma concentrations are handled as described in Section 7.4.1.

7.6 FURTHER OBJECTIVE ANALYSIS

Independent of the further objectives stated in the CTP, this section describes details of the further endpoint analyses outlined in the CTP.

[redacted]

7.6.2 Safety parameters

Safety and tolerability endpoints will be analysed as described in Section 7.8 of this TSAP.

7.7 EXTENT OF EXPOSURE

The date and time of drug administration will be listed for each subject.

7.8 SAFETY ANALYSIS

All safety analyses will be performed on the treated set.

7.8.1 Adverse Events

AEs will be coded with the most recent version of MedDRA. The coding version number will be displayed as a footnote in the respective output.

The analyses of AEs will be descriptive in nature. All analyses of AEs will be based on the number of subjects with AEs and not on the number of AEs.

For further details on summarization of AE data, please refer to "Analysis and Presentation of Adverse Event Data from Clinical Trials" (6) and "Handling of missing and incomplete AE dates" (3).

The analysis of AEs will be based on the concept of treatment emergent AEs. That means that all AEs will be assigned to screening, on-treatment phase and follow-up phase as defined in Section 6.1. AEs will be analysed based on treatments as defined in Table 6.1: 1.

An overall summary of AEs will be presented. This overall summary will comprise summary statistics for the class of AESIs.

CTP: *The following are considered as AESIs:*

- *Potential severe DILI*
  A potential severe Drug Induced Liver Injury (DILI) that requires follow-up is defined by the following alterations of hepatic laboratory parameters:
    - *An elevation of AST (aspartate aminotransferase) and/or ALT (alanine aminotransferase) ≥3-fold ULN combined with an elevation of total bilirubin ≥2-fold ULN measured in the same blood sample, or in samples drawn within 30 days of each other, or*
    - *Aminotransferase (ALT, and/or AST) elevations ≥10-fold ULN*

The investigator had to classify on the eCRF whether an observed AE was an AESI or not.

According to ICH E3 (7), in addition to Deaths and Serious Adverse Events, 'other significant' AEs need to be listed in the clinical trial report. These will be any non-serious adverse event that led to an action taken with study drug (e.g. discontinuation or dose reduced or interrupted).

The frequency of subjects with AEs will be summarised by treatment (cohort), primary SOC and preferred term. AEs which were considered by the investigator to be drug related will be summarised separately. Separate tables will also be provided for subjects with SAEs and subjects with AESIs. AEs will also be summarised by maximum intensity.

The SOCs and preferred terms within SOCs will be sorted by descending frequency over all treatment groups.

For disclosure of AE data on ClinicalTrials.gov, the frequency of subjects with non-serious AEs occurring with an incidence of greater than 5 % (in preferred terms) will be summarised

by treatment (cohort), primary SOC and preferred term. The frequency of subjects with SAEs will also be summarised.

For disclosure of AE data in the EudraCT register, the frequency of AEs, the frequency of non-serious AEs with an incidence of greater than 5 % (in preferred terms) and the frequency of SAEs will be summarised.

For support of lay summaries, the frequency of subjects with drug-related SAEs will be summarised by treatment (cohort), primary SOC and preferred term.

7.8.2 Laboratory data

The analyses of laboratory data will be descriptive in nature and will be based on BI standards (8).

Analyses will be based on normalised values, which means transforming to a standard unit and a standard reference range. The original values will be analysed if the transformation into standard unit is not possible for a parameter.

Descriptive statistics of laboratory values over time and for the difference from baseline (see Section 6.7) will be provided. Frequency tables of changes between baseline and last value on treatment with respect to the reference range will be presented.

Unscheduled measurements of laboratory data will be assumed to be repeat measurements of the most recent scheduled measurement (e.g. for follow-up or confirmation of a particular value). Therefore, unscheduled measurements will be assigned to the planned time point of the previous scheduled measurement. Descriptive statistics will be calculated by planned time point based on the worst value of the subject at that planned time point (or assigned to that planned time point).

Clinically significant abnormal laboratory values are only those identified either in the Investigator's comments or at the Report Planning Meeting at the latest. It is the Investigator's responsibility to decide whether a lab value is clinically significant abnormal or not.

Laboratory data will be compared to their reference ranges. Values outside the reference range will be highlighted in the listings.

Clinically relevant findings in laboratory data will be reported as baseline conditions (prior to administration of study drug) or as AEs (after administration of study drug) if judged clinically relevant by the investigator, and will be analysed as such.

7.8.3 Vital signs

Only descriptive statistics are planned for this section of the report. Descriptive statistics of vital signs over time and for the difference from baseline (see Section 6.7) will be provided.

Unscheduled measurements of vital signs will be assigned to planned time points in the same way as described above for laboratory data. However, for vital signs, descriptive statistics will be calculated by planned time point based on the last value of the subject at that planned time

point (or assigned to that planned time point). If the time of measurement is missing for a scheduled measurement, the scheduled measurement will be used in calculation of descriptive statistics (as time difference between scheduled and unscheduled cannot be assessed).

If the time of measurement is missing for an unscheduled measurement, this measurement will be listed but will be ignored for the calculation of descriptive statistics.

Clinically relevant findings in vital signs data will be reported as baseline conditions (prior to first administration of study treatment) or as AEs (after first administration of study treatment) if judged clinically relevant by the investigator, and will be analysed as such.

7.8.4 ECG

Abnormal findings in ECG will be reported as baseline conditions (at screening) or as AEs (during the trial) if judged clinically relevant by the investigator, and will be analysed as such. No separate listing or analysis of ECG data will be prepared.

7.9 OTHER ANALYSIS

7.9.1 Physical examination

Physical examination findings will be reported as relevant medical history/baseline condition (if a condition already exists before first administration of study treatment) or as AE (if condition emerges after first administration of study treatment) and will be summarised as such. No separate listing or analysis of physical examination findings will be prepared.

7.9.2 Body weight

Body weight will only be listed.

8. TIMEPOINT OF RELEASE OF TREATMENT INFORMATION

The treatment information will be loaded into the trial database as requested during study conduct.

9. REFERENCES

1.	*CPMP/ICH/363/96:* "Statistical Principles for Clinical Trials", ICH Guideline Topic E9, Note For Guidance on Statistical Principles for Clinical Trials, current version.
2.	BI-VQD-12045_40-413: "Identify and Manage Important Protocol Deviations (iPD)", current version; KMED
3.	KM Asset BI-KMED-BDS-HTG-0035: "Handling of missing and incomplete AE dates", current version; KMED
4.	KM Asset BI-KMED-TMCP-MAN -0014: "Noncompartmental PK/PD Analyses of Clinical Studies", current version; KMED
5.	KM Asset BI-KMED-BDS-HTG-0045: "Standards for Reporting of Clinical Trials and Project Summaries", current version; KMED
6.	KM Asset BI-KMED-BDS-HTG-0066: "Analysis and Presentation of Adverse Event Data from Clinical Trials", current version; KMED
7.	CPMP/ICH/137/95: "Structure and Content of Clinical Study Reports", ICH Guideline Topic E3; Note For Guidance on Structure and Content of Clinical Study Reports, current version
8.	KM Asset BI-KMED-BDS-HTG-0042: "Handling, Display and Analysis of Laboratory Data", current version; KMED
9.	KM Asset BI-KMED-TCMP-MAN-0010: "Description of Analytical Transfer Files, PK/PD Data Files and ADA files", current version; KMED

11. HISTORY TABLE

Table 11: 1 History table

Version	Date (DD-MMM-YY)	Author	Sections changed	Brief description of change
1.0	**08-Dec-23**	[redacted]	None	This is the final TSAP.