TRIAL STATISTICAL ANALYSIS PLAN

c38962518-01

BI Trial No.:	1346-0035
Title:	The effect of multiple oral doses of BI 425809 on metabolism of midazolam administered orally in healthy male subjects (open-label, two-period, one-sequence trial)
Investigational Product(s):	BI 425809
Responsible trial statistician(s):	[redacted] Phone: +[redacted]
Date of statistical analysis plan:	10 AUG 2022 SIGNED
Version:	1

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2. LIST OF ABBREVIATIONS

See Medicine Glossary:
http://glossary

Term	Definition / description
ADS	Analysis data set
AE	Adverse Event
AESI	Adverse event of special interest
ANOVA	Analysis of variance
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
$AUC_{0-\infty}$	Area under the concentration-time curve of the analyte in plasma over the time interval from 0 extrapolated to infinity
AUC_{0-tz}	Area under the concentration-time curve of the analyte in plasma over the time interval from 0 to the last quantifiable data point
BI	Boehringer Ingelheim
BMI	Body mass index
BP	Blood pressure
CARE	Clinical data analysis and reporting environment
CDR	Clinical Data Repository
CI	Confidence interval
C_{max}	Maximum measured concentration of the analyte in plasma
C_{pre}	Predose plasma concentration
COVID	Coronavirus disease
CRF	Case Report Form, paper or electronic (sometimes referred to as 'eCRF')
CSD	Company Standard Displays
CTP	Clinical Trial Protocol
CTR	Clinical Trial Report
C-SSRS	Columbia-Suicidal Severity Rating Scale
CV	Arithmetic coefficient of variation
DILI	Drug-induced liver injury
ECG	Electrocardiogram
EDMS	Electronic Document Management System

Term	Definition / description
EudraCT	European union drug regulating authorities clinical trials
gCV	geometric coefficient of variation
gMean	Geometric mean
ICH	International Conference On Harmonisation
iPD	Important protocol deviations
ISF	Investigator Site File
max	Maximum
MDZ	midazolam
MedDRA	Medical Dictionary For Regulatory Activities
min	Minumum
N	Number of non-missing observations
P10	10^{th} percentile
P90	90^{th} percentile
PK	Pharmacokinetics
PKS	Pharmacokinetic parameter analysis set
PR	Pulse rate
Q1	1^{st} quartile
Q3	3^{rd} quartile
R	Reference treatment
RAGe	Report appendix generator
REP	Residual Effect Period
RPM	Report Planning Meeting
SAE	Serious adverse event
SD	Standard Deviation
SDL	Subject Data Listing
SOC	System Organ Class
T	Test treatment
TMF	Trial Master File
TS	Treated set
TSAP	Trial Statistical Analysis Plan
ULN	Upper limit of normal range
WHO-DD	World Health Organization Drug Dictionary

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.

Study data (including data entered in the RAVE EDC system and external data provided by suppliers) will be stored in a Clinical Data Repository (CDR).

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).

Pharmacokinetic (PK) parameters will be calculated using Phoenix WinNonlin™ software (version 8.1.1 or higher, [redacted]).

4. CHANGES IN THE PLANNED ANALYSIS OF THE STUDY

All analyses as planned in the CTP will be performed and are described in more detail in this TSAP.

5. ENDPOINTS(S)

5.1 PRIMARY ENDPOINT(S)

Section 2.1.2 of the CTP:

The following pharmacokinetic parameters will be determined for midazolam:

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

5.2 SECONDARY ENDPOINT(S)

5.2.1 Key secondary endpoint(s)

This section is not applicable as no key secondary endpoints have been defined in the CTP.

5.2.2 Secondary endpoint(s)

Section 2.1.3 of the CTP:

The following pharmacokinetic parameter will be determined for midazolam:

- *$AUC_{0-\infty}$ (Area under the concentration-time curve of midazolam in plasma over the time interval from 0 extrapolated to infinity)*

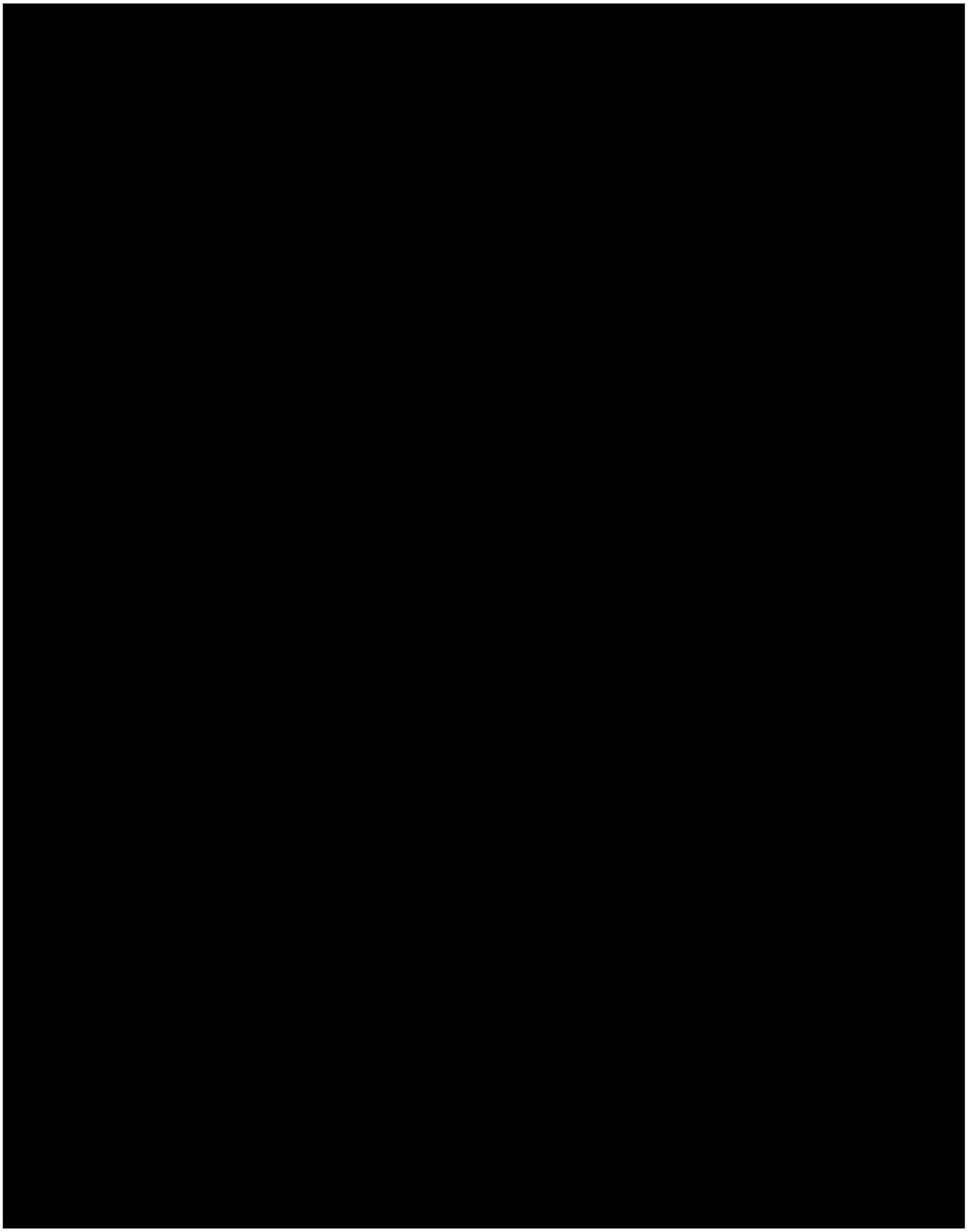
5.3 FURTHER ENDPOINT(S)

5.3.1 Safety parameters

Section 2.2.2.4 of the CTP:

Safety and tolerability […]will be assessed based on:

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



6. GENERAL ANALYSIS DEFINITIONS

6.1 TREATMENT(S)

For basic study information on investigational products and selection of doses, please see CTP Sections 3 and 4.

Section 3.1 of the CTP:

The trial will be performed as a non-randomised, open-label, two-period trial in healthy male subjects in order to compare the test treatment (T) to the reference treatment (R) using one-sequence R-T.

For details of dosage and formulation see below:

Table 6.1: 1 Treatments and labels used in the analysis

Treatment		Short label
R	midazolam, 2mg, solution	MDZ
T	BI 425809 10 mg, tablet + midazolam, 2mg, solution	BI+MDZ

The sequence for "R-T" is named "MDZ / BI+MDZ" accordingly.

Section 1.2.3 of the CTP: *The Residual Effect Period (REP) of BI 425809 is 11 days. This is the period after the last dose during which measurable drug levels and/or pharmacodynamic effects are still likely to be present. The residual effect period of midazolam is 12 hours.*

The following study phases will be defined for the analysis of adverse events (AEs):

Table 6.1: 2 Analysis phases for statistical analysis of AEs, and actual treatment for analysis of laboratory data, vital signs and ECG for SRD part

Study analysis phase	Short Label	Start	End
Screening[1]	**Screening**	0:00h on date of informed consent	Date/time of administration of midazolam in treatment period 1
On treatment	**MDZ**	Date/time of administration of midazolam alone in treatment period 1	12 hours after date/time of administration of midazolam in treatment period 1 (End of REP of midazolam) OR Date/time of first administration of BI 425809 in treatment period 2 OR Date/time of trial termination – whatever occurs first
On treatment	**BI**	Date/time of first administration of BI 425809 alone in treatment period 2	Date/time of administration of midazolam in treatment period 2 OR Date/time of trial termination – whatever occurs first
On treatment	**BI+ MDZ**	Date/time of administration of midazolam in treatment period 2	11 days = 264h after date/time of administration of midazolam in treatment period 2 (End of REP of BI 425809) OR Date/time of trial termination – whatever occurs first
Follow-up	**FU MDZ**	Date/time of administration of midazolam alone in treatment period 1 + 12 h thereafter	Date/time of first administration of BI 425809 in treatment period 2 OR Date/time of trial termination – whatever occurs first
Follow-up	**FU BI+MDZ**	Date/time of administration of midazolam in treatment period 2 + 11 days (264h)	12:00 a.m. on day after trial termination date

Section 7.2.5 of the CTP: *Note that AEs occurring after the last per protocol contact* but entered before final database lock *will be reported to Pharmacovigilance only and will not be captured in the trial database.*

The following AE displays will be provided in the report:

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

In these displays (AE summary tables), the on treatment phase will be analysed (labelled with the name of the study treatment (short label) as in Table 6.1:2). Screening and follow-up periods will not be included in this analysis.
The following total will be provided in addition (Section 15.3 only):

- a total over all on treatment phases included in this analysis ("**Total on treatment**")

B) Section 15.4 of the CTR displays:

- Screening
- On treatment (labelled with the name of the study treatment (short label) as in Table 6.1:2)
- Follow-up MDZ (labelled "**FU MDZ**")
- Follow-up BI+MDZ(labelled "**FU BI+MDZ**")

In Section 16.1.13.1.8 AE tables, the following totals will be provided in addition:

- a total over all on treatment phases ("**Total on treatment** ")

For detailed information on the handling of the treatments refer to Technical TSAP ADS plan and Analysis Data Reviewers guide.

6.2 IMPORTANT PROTOCOL DEVIATIONS

Documentation of iPD categories and handling of iPDs in analysis is included in the DV domain specifications and stored within the TMF in EDMS. The iPDs will be summarized and listed in the CTR.
Non-important COVID-19 related protocol deviations will only be listed.

6.3 SUBJECT SETS ANALYSED

The treated set (TS) and pharmacokinetic parameter analysis set (PKS) will be used as defined in **Section 7.2.1.1 of the CTP:**

- *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 specified in the following subsection 'Pharmacokinetics'). 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 and model-based analyses of PK parameters will be based on the PKS.

In the following table, it is defined which subject set is used for which class of endpoint:

Table 6.3: 1 Subject sets analysed

	Subject set	
Class of endpoint	TS	PKS
Disposition	X	
iPD	X	
Primary endpoints		X
Secondary endpoint		X
Further PK endpoints, incl. steady state analysis		X
[redacted]		[redacted]
Safety parameters	X	
Demographic/baseline characteristics	X	
Treatment exposure	X	

[redacted]

6.5 POOLING OF CENTRES

This section is not applicable, because the study was performed in only one centre.

6.6 HANDLING OF MISSING DATA AND OUTLIERS

Handling of missing data and outliers will be performed as described in **Section 7.3.1 and 7.3.2 of the CTP.**

Section 7.3.1 of the CTP: *It is not planned to impute missing values for safety parameters.*

The only exceptions where imputation might be necessary for safety evaluation are AE dates. Missing or incomplete AE dates are imputed according to BI standards (see "Handling of Missing and Incomplete AE Dates" (2)).

Section 7.3.2 of the CTP:

Handling of missing PK data will be performed according to the relevant BI internal procedures.

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

Missing data and outliers of PK data are handled according to BI standards (see "Standards and processes for analyses performed within Clinical Pharmacokinetics/Pharmacodynamics" (3) and "Noncompartmental PK/PD Analyses of Clinical Studies" (4)).

[redacted]

6.7 BASELINE, TIME WINDOWS AND CALCULATED VISITS

Section 7.2.5 of the CTP: *For laboratory data, ECG and vital signs, baseline is defined as the last measurement before first intake of BI 425809.*

[redacted]

Time windows are defined in **Section 6.1 of the CTP**. Adherence to time windows will be checked via the consistency check listings at the RPM.

Unscheduled measurements of laboratory data, vital signs 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.

7. PLANNED ANALYSIS

The format of the listings and tables will follow the BI guideline "Standards for Reporting of Clinical Trials and Project Summaries" (6).

The individual values of all subjects will be listed. Listings will be sorted by subject number, visit and time point (if visit/ time point is applicable in the respective listing). AE listings will be sorted by assigned treatment (see Section 7.8.1 below 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 non-missing observations
Mean	arithmetic mean
SD	standard deviation
Min	minimum
Median	median
Max	maximum

For plasma 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

The data format for descriptive statistics of concentrations will be identical to 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 (unless otherwise specified, all subjects in the respective subject set whether they have non-missing values or not).

Percentages will be given in integer numbers due to the small sample size of <100. Percentages will be based on all subjects in the respective subject set whether they have non-missing values or not. The category missing will be displayed only if there are actually missing values.

Exclusion of PK parameters

The ADS “ADPP” (PK parameters) contains column variables APEXC and APEXCO indicating inclusion/exclusion (APEXC) of a PK parameter and an analysis flag comment

(APEXCO). All analyses based on the PKS will include parameters if they are not flagged for exclusion, that is APEXC is equal to "Included".

Exclusion of PK concentrations

The ADS "ADPC" (PK concentrations per time-point or per time-interval) contains column variables ACEXC and ACEXCO indicating inclusion/exclusion (ACEXC) 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.
- 'DESC STATS' the value will be excluded from descriptive evaluations per planned time point/time interval.
- 'HALF LIFE', the value will be excluded from half-life calculation (and, as a consequence, any calculation that relies on λ_z) only; the value is included for all other analyses.

If ACEXCO contains the addition 'TIME VIOLATION' or 'TIME DEVIATION' the value can be used for further analyses based on actual times. Excluded concentration itself will be listed in the CTR associated with an appropriate flag.

Further details are given in "Noncompartmental PK/PD Analyses of Clinical Studies" (4) and "Description of Analytical Transfer Files, PK/PD Data files and ADA files" (5).

7.1 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

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

7.2 CONCOMITANT DISEASES AND MEDICATION

Descriptive statistics are planned for this section of the CTR, based on the TS.

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.

In the remaining document 'therapy' will be used for non-drug therapies and concomitant medications.

Section 7.2.5 of the CTP: *Previous and concomitant therapies will be presented per treatment group without consideration of time intervals and treatment periods.*

A therapy 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 diagnoses and therapies will be listed. Subjects without any concomitant disease or concomitant therapy should be marked with a "No" in the respective column.

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

7.3 TREATMENT COMPLIANCE

Section 4.3 of the CTP: *Compliance will be assured by administration of all trial medication in the trial centre under supervision of the investigating physician or a designee. The measured plasma concentrations of trial medication will provide additional confirmation of compliance.*

Treatment compliance will not be analyzed or listed as a specific endpoint, but judged by observed analyte concentrations. Any deviation from complete medication intake will be addressed in the RPM (see Section 6.2) and described in the CTR.

7.4 PRIMARY ENDPOINT(S)

7.4.1 Primary analysis of the primary endpoint(s)

Section 7.2.2 of the CTP:

Primary analyses

The statistical model used for the analysis of the primary endpoints will be an analysis of variance (ANOVA) model on the logarithmic scale. That is, the PK endpoints will be log-

transformed (natural logarithm) prior to fitting the ANOVA model. This model will include effects accounting for the following sources of variation: subject and treatment. The effect 'subjects' will be considered as random, whereas the 'treatment' effect will be considered as fixed. The model is described by the following equation:

$y_{km} = \mu + s_m + \tau_k + e_{km}$, *where*

y_{km} = *logarithm of response measured on subject m in receiving treatment k,*

μ = *the overall mean,*

s_m = *the effect associated with the* m^{th} *subject, m = 1, 2, ..., 15*

τ_k = *the* k^{th} *treatment effect, k = 1, 2,*

e_{km} = *the random error associated with the* m^{th} *subject who received treatment k,*

where $s_m \sim N(0, \sigma_B^2)$ *i.i.d.,* $e_{km} \sim N(0, \sigma_W^2)$ *i.i.d. and* s_m, e_{km} *are independent random variables.*

Point estimates for the ratios of the geometric means (test/reference) for the primary endpoints (see Section 5.1) *[...] and their two-sided 90% confidence intervals (CIs) will be provided.*

For each endpoint, the difference between the expected means for log(T)-log(R) will be estimated by the difference in the corresponding adjusted means (Least Squares Means). Additionally their two-sided 90% confidence intervals will be calculated based on the residual error from the ANOVA and quantiles from the t-distribution. These quantities will then be back-transformed to the original scale to provide the point estimate and 90% CIs for each endpoint.

The implementation for this analysis will be accomplished by using the CSD macros based on PKS.

[redacted]

7.5 SECONDARY ENDPOINT(S)

7.5.1 Key secondary endpoint(s)

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

7.5.2 (Other) Secondary endpoint(s)

Section 7.2.3 of the CTP: *The secondary endpoint* […] $AUC_{0-\infty}$ *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.*

[redacted]

7.7 EXTENT OF EXPOSURE

Descriptive statistics of number of doses and calculated total doses of BI 425809 and midazolam are planned for this section of the CTR based on the TS. The date and time of drug administrations will be listed for each subject.

7.8 SAFETY ANALYSIS

Section 7.2.5 of the CTP: *For all analyses, the treatment actually administered (= treatment at onset) to the subject will be used (any deviations from the assigned treatment will be discussed in the minutes of the Report Planning Meeting).*

7.8.1 Adverse Events

AEs will be coded with the most recent version of MedDRA.

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 – Display Template" (7) and "Analysis and Presentation of AE data from clinical trials" (8).

The analysis of AEs will be based on the concept of treatment emergent AEs. That means that all AEs will be assigned to screening or on-treatment periods as defined in Section 6.1. AEs will be analysed based on actual 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.

Section 5.2.6.1.4 of the 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*

  These lab findings constitute a hepatic injury alert and the subjects showing these lab abnormalities need to be followed up according to the 'DILI checklist' provided in the ISF. In case of clinical symptoms of hepatic injury (icterus, unexplained encephalopathy, unexplained coagulopathy, right upper quadrant abdominal pain, etc.) without lab results (ALT, AST, total bilirubin) available, the Investigator should make sure that these parameters are analysed, if necessary in an unscheduled blood test. Should the results meet the criteria of hepatic injury alert, the procedures described in the DILI checklist should be followed.

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

According to ICH E3 (9), 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, 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.

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, 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 summarized.

For support of lay summaries, the frequency of subjects with drug-related SAEs will be summarized by treatment, 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 "Handling, Display and Analysis of Laboratory Data" (10).

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 by treatment.

Laboratory data will be analysed qualitatively via comparison to their reference ranges. Values outside the reference range as well as possibly clinically significant values will be highlighted in the listings. Possibly clinically significant abnormal laboratory values will be listed in Section 15.4.1.

It is the Investigator's responsibility to decide whether a lab value is clinically significant abnormal or not. Clinically significant abnormal laboratory values are identified either in the Investigator's comments or at the Report Planning Meeting at the latest. They will be reported or as AEs (after first administration of study treatment).

7.8.3 Vital signs

Vital signs (blood pressure and pulse rate) will be analysed descriptively.

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 analyzed as such.

7.8.4 ECG

ECG recordings will be checked by the investigator for pathological results. Clinically relevant abnormal findings for ECG will be listed under 'Relevant Medical History / Baseline Conditions' (when they occurred during screening) or will be reported as AEs (when they occurred during treatment), and will be analysed as such. No separate ECG listing will be provided.

7.8.5 Others

7.8.5.1 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 summarized as such. No separate listing or analysis of physical examination findings will be prepared.

7.8.5.3 Body weight

Since body weight is only assessed at screening it will only be listed.

7.8.5.4 Suicidality assessment (C-SSRS)

Only findings will be listed.

Section 7.2.5 of the CTP: *Results regarding the C-SSRS will only be listed.*

8. TIMEPOINT OF RELEASE OF TREATMENT INFORMATION

The treatment information will be loaded into the trial database at trial initiation.

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-KMED-BDS-HTG-0035:* "Handling of Missing and Incomplete AE Dates", current version, KMED.
3.	*BI-KMED-TMCP-MAN-0012*: "Standards and processes for analyses performed within Clinical Pharmacokinetics/Pharmacodynamics", current version, KMED.
4.	*BI-KMED-TMCP-MAN-0014*: "Noncompartmental PK/PD Analyses of Clinical Studies", current version, KMED.
5.	*BI-KMED-TMCP-MAN-0010*: "Description of Analytical Transfer Files, PK/PD Data files and ADA files", current version, KMED.
6.	BI-KMED-BDS-HTG-0045: "Standards for Reporting of Clinical Trials and Project Summaries", current version; KMED.
7.	*BI-KMED-BDS-HTG-0041*: "Analysis and Presentation of Adverse Event Data from Clinical Trials – Display Template", current version; KMED.
8.	*BI-KMED-BDS-HTG-0066*: "Analysis and Presentation of AE data from clinical trials", current version, KMED.
9.	*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, EMA webpage.
10.	*BI-KMED-BDS-HTG-0042*: "Handling, Display and Analysis of Laboratory Data", current version, KMED.

[redacted]

11. HISTORY TABLE

Table 11: 1 History table

Version	Date (DD-MMM-YY)	Author	Sections changed	Brief description of change
1	**10-AUG-22**	[redacted]	None	This is the final TSAP