TRIAL STATISTICAL ANALYSIS PLAN

c23146709-03

BI Trial No.:	1336-0011
Title:	An open label phase Ib dose finding study of BI 836880 in combination with ezabenlimab to characterize safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy in patients with locally advanced or metastatic non-squamous Non-Small Cell Lung Cancer and in other solid tumors Including Protocol Amendment 8 [c16151514-11]
Investigational Product(s):	BI 836880 Ezabenlimab (BI 754091)
Responsible trial statistician(s):	[redacted] Phone: [redacted] Fax: [redacted]
Date of statistical analysis plan:	6 Jun 2022
Version:	3.0

1. TABLE OF CONTENTS

[redacted]

LIST OF TABLES

2. LIST OF ABBREVIATIONS

Term	Definition / Description
AE	Adverse Event
[redacted]	[redacted]
BHM	Bayesian Hierarchical Model
BOR	Best Overall Response
CR	Complete Response
CTC	Common Terminology Criteria
CTP	Clinical Trial Protocol
CTR	Clinical Trial Report
[redacted]	[redacted]
DM&SM	Boehringer Ingelheim Data Management And Statistics Manual
DLT	Dose Limiting Toxicity
DoR	Duration of Response
DRA	Drug Regulatory Affairs
DMG	Dictionary Maintenance Group
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EMEA	European Agency For The Evaluation Of Medicinal Products
FAS	Full Analysis Set
GBM	Glioblastoma
GEP	Gene-Expression Profile
ICH	International Conference On Harmonisation
IPD	Important Protocol Deviation
[redacted]	[redacted]
LOCF	Last Observation Carried Forward
MedDRA	Medical Dictionary For Regulatory Activities
MQRM	Medical Quality Review Meeting
NOA	Not Analysed
NOR	No Valid Result
NOS	No Sample
NSCLC	Non-Small Cell Lung Cancer
OR	Objective Response

Term	Definition / Description
OS	Overall Survival
PD	Protocol Deviation
PFS	Progression-Free Survival
PFS6	Six-Month Progression-Free Survival
PK	Pharmacokinetics
PKS	PK Analysis Set
PPS	Per Protocol Set
PR	Partial Response
PSTAT	Project Statistician
PT	Preferred Term
Q1	Lower Quartile
Q3	Upper Quartile
RANO	Response Assessment in Neuro-Oncology
RECIST	Response Evaluation Criteria In Solid Tumours
REP	Residual Effect Period
RP2D	Recommended Phase 2 Dose
RPM	Report Planning Meeting
SA	Statistical Analysis
SD	Standard Deviation
SMC	Safety Monitoring Committee
SMQ	Standardized MedDRA Query
SOC	System Organ Class
SSC	Special Search Category
TCM	Trial Clinical Monitor
TESS	Treatment Emergent Signs And Symptoms
ToC	Table of Contents
TMW	Trial Medical Writer
TS	Treated Set
TSAP	Trial Statistical Analysis Plan
[redacted]	[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, and randomization.

SAS® Version 9.4 or the latest version will be used for analyses.

R Version 3.5.1 and JAGS Version 4.3.0 or the latest versions will be used for the BLRM and BHM analyses.

5. ENDPOINT(S)

This is a Phase Ib study containing two parts: Part 1 (dose escalation of BI 836880 in combination with ezabenlimab (BI 754091)) and Part 2 (expansion at the RP2D in 8 cohorts with different tumour types and line of therapy) in patients with locally advanced or metastatic non-squamous NSCLC and in other solid tumors.

The primary objective for Part 1 is to determine the safety and tolerability of BI 836880 in combination with ezabenlimab and find the Maximum Tolerated Dose (MTD)/Recommended Phase 2 Dose (RP2D).

The primary objective for Part 2 is to assess the anti-tumor activity of BI 836880 in combination with ezabenlimab in patients with locally advanced or metastatic non-squamous NSCLC and in other solid tumors.

5.1 PRIMARY ENDPOINT(S)

PART 1:
The primary endpoint is the number of patients with dose limiting toxicities (DLTs) within the MTD evaluation period, which will be assessed for dose escalation in order to determine the maximum tolerated dose (MTD) of the combination of BI 836880 and ezabenlimab.

The MTD is defined as the highest dose with less than 25% risk of the true DLT probability being above 33% and may be considered reached if the probability that the true DLT rate is in the target interval (16%-33%) is sufficiently large during the MTD evaluation period.

The definition of DLTs for solid tumour patients is provided in Section 5.2.6.1 of the CTP.

The MTD evaluation period is defined as the time from the first administration of study treatment to the start of the second treatment cycle, i.e., the first treatment cycle.

PART 2:
The primary endpoint is Objective Response (OR) defined as best overall response (RECIST 1.1) of complete response (CR) or partial response (PR) from first treatment infusion until the earliest of disease progression, death, or last evaluable tumor assessment before start of subsequent anti-cancer therapy, lost to follow-up, or withdrawal of consent. In the case of recurrent glioblastoma (GBM), tumour assessment will be based on RANO (Response Assessment in Neuro-Oncology) criteria.

5.2 SECONDARY ENDPOINT(S)

5.2.1 Key secondary endpoint(s)

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

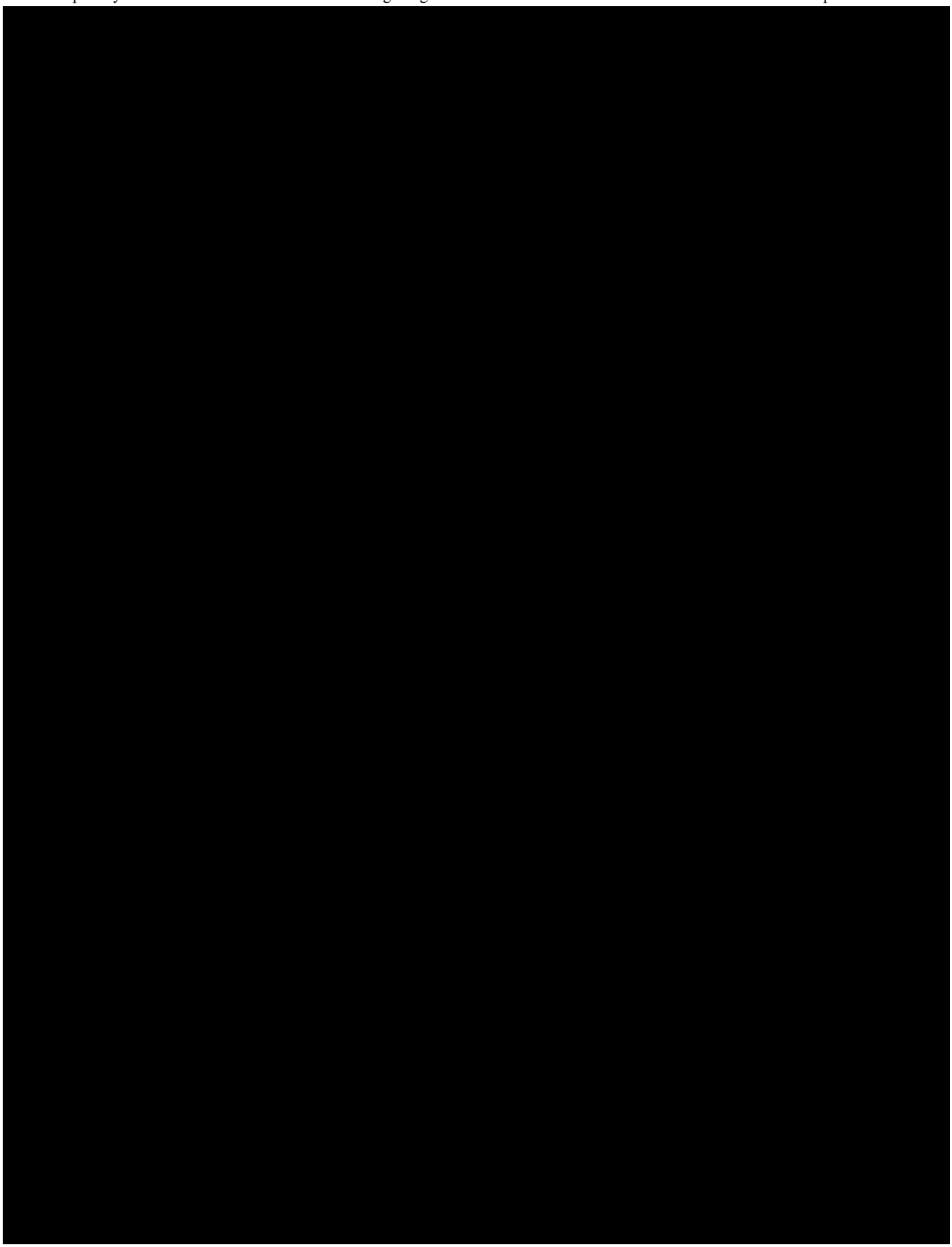
5.2.2 Secondary endpoint(s)

PART 1:

- Adverse events (AEs), drug related AEs, drug related AEs leading to discontinuation during treatment period.
- Pharmacokinetic parameters C_{max}, T_{max}, and $AUC_{0\text{-}504h}$ after the first and fourth infusion cycle.

PART 2:

- Adverse events (AEs), drug related AEs, drug related AEs leading to discontinuation during treatment period.
- Disease control (DC), defined as best overall response of CR, PR, or stable disease (SD) by RECIST 1.1 (RANO for the GBM cohort) from start of treatment infusion until the earliest of disease progression, death, or last evaluable tumor assessment before start of subsequent anti-cancer therapy, lost to follow-up, or withdrawal of consent.
- Duration of objective response (DoR), defined as the time from first documented CR or PR by RECIST 1.1 (RANO for the GBM cohort) until the earliest of disease progression or death among patients with OR.
- Progression-free survival (PFS) (RANO for the GBM cohort and RECIST 1.1 for all other cohorts), defined as the time from first treatment infusion until disease progression or death from any cause, whichever occurs earlier.
- Tumor shrinkage (in millimeters), defined as the difference between the minimum post-baseline sum of diameters of target lesions (longest for non-nodal lesions, short axis for nodal lesions) and the baseline sum of diameters of the same set of target lesions. In GBM, using RANO criteria, tumor shrinkage will be calculated based on the difference between the post-baseline and baseline measurements of the sum of product of the largest bi-dimensional measurements for all target lesions.
- Pharmacokinetic parameters C_{max}, T_{max}, and $AUC_{0\text{-}504h}$ after the first infusion cycle.



6. GENERAL ANALYSIS DEFINITIONS

6.1 TREATMENT(S)

In this open-label Phase Ib trial, treatments are not randomized. In the dose escalation part (Part 1), the starting dose combination is BI 836880 360 mg + ezabenlimab (BI 754091) 240 mg every three weeks. Dose escalation is only performed for BI 836880. Ezabenlimab is fixed at dose 240 mg. Dose escalation decisions will be made by the Safety Monitoring Committee (SMC). Based on the dose escalation data in Part 1, the SMC will select one combination dose for the expansion cohorts in Part 2. Data of the dose expansion part (Part 2) will be displayed separately for each of the multiple cohorts.

For the dose escalation part (Part 1), the initial trial medication (i.e., dose level) assigned at the beginning of the first treatment cycle will be used as the label of the analysing treatment.

For safety analyses, adverse events (AEs) will be displayed separately within the following time periods: “Screening”, “On-treatment”, or “Post-study” (see Table 6.1: 1). This will be applied for both AEs and immune-related AEs. Refer to CTP Section 5.2.7.2 for details of AE collection and reporting.

Table 6.1: 1 Definition of treatment periods

Analysing Treatment Period	Start Date (including)	Stop Date (excluding)
Screening	Date of informed consent	The date of first trial medication administration - 1 day
On-treatment	Date of first administration of trial medication	Date of last trial medication administration + REP, or death, or DBL date, whichever comes first i.e., actual on-treatment period + REP,
Post-study	Last day of on-treatment period +1 day	Date of the last contact date or death, or DBL date, whichever comes first

Note: A 42-day residual effect period (REP) is defined for both Parts 1 and 2.

6.2 IMPORTANT PROTOCOL DEVIATIONS

A protocol deviation (PD) is important if it affects the rights or safety of the study patients, or if it can potentially influence the primary outcome measurements in a non-negligible way. Important protocol deviations (IPDs) are stored in the DV domain template (Excel spreadsheet). IPDs will be reviewed at Medical Quality Review Meetings (MQRMs) conducted periodically during the trial. A list of PDs will be discussed at the report planning meetings (RPMs).

If the data show other IPDs, this table will be supplemented accordingly at MQRMs or RPMs or through team review of the manual PD log. The final list of IPDs will be confirmed at the

last RPM before DBL. The decision whether a patient will be excluded from the analysis will be made at the final RPM prior to DBL.

Patients with an IPD will be identified and reported in the CTR. In addition, a per protocol set excluding patients with IPDs that could potentially impact the evaluation of the primary endpoint(s) may be defined. Primary endpoint analysis may be performed based on the per protocol set in addition to the treated set.

6.3 SUBJECT SETS ANALYSED

Screened Set (SCS)

This patient set includes all patients who have signed the informed consent. The screened set will be used for patient disposition tables.

Treated set (TS)

This patient set includes all patients enrolled in the trial who were documented to have received at least one dose of ezabenlimab or BI 836880. The TS is used for both efficacy analysis and safety analyses.

MTD set

This patient set includes all patients enrolled in dose escalation and confirmation of MTD cohort of the trial (Part 1) who were documented to have received at least one dose of ezabenlimab or BI 836880and were evaluable for the MTD determination.

Expansion cohort treated set

This patient set includes all patients enrolled in the expansion part (Part 2) and were documented to have received at least one dose of ezabenlimab or BI 836880.

PK analysis set (PKS)

This patient set includes all patients in the TS who provide at least one evaluable observation for at least one PK endpoint and no PK relevant protocol deviation. PKS is used for statistical PK analysis.

[redacted]

6.5 POOLING OF CENTRES

This section is not applicable because centre is not included in the statistical model.

6.6 HANDLING OF MISSING DATA AND OUTLIERS

Missing or incomplete AE dates are imputed according to BI standards (see “Handling of missing and incomplete AE dates”) (3). Missing data and outliers of PK data are handled according to (2). Please refer to Section 7.5 of the CTP for more details. According to (2), missing biomarker data (NOS - no sample, NOR - no valid result, NOA - not analyzed) will not be imputed. Handling of data below or above the limit of quantification, e.g., the myriad panel data:

- BLQ data will be replaced by ½ LLOQ.

- ALQ data will be replaced by ULOQ, if ULOQs are available. Otherwise, ALQ data will be excluded from the analysis.

6.7 BASELINE, TIME WINDOWS AND CALCULATED VISITS

Visit labels

Study days and visits will be labelled according to the flow charts in the CTP. The visit schedule with accompanying details can also be found in the flow charts in the CTP.

Definition of "baseline"

For laboratory values, the baseline value is the most recently observed value before or on the first day of infusion of trial medication; for laboratory measurements, the examination time may also need to be considered, in instances where time is recorded in addition to date. For all other data values, baseline is defined as the most recent measurement taken prior to first administration of trial medication. If not available, then the values reported at the screening visit will be considered.

Time windows

Time windows and visits will be calculated to determine the planned day of tumour measurement and response status based on the protocol-specified tumour imaging schedule. Imaging data will be displayed as: Screening, Week 6, Week 12, Week 18, etc. The number of weeks will be calculated using their relative day (from start of treatment) using a ±3 week window. (Images taken in the first 3 weeks from start of treatment will be assigned to Week 6.) Images which are not older than 28 days at start of treatment will be sufficient as screening images and do not need to be repeated.

How to include measurements taken between time windows

The same visit windows will be used for safety laboratory and vital sign assessments. If there are multiple safety or laboratory values in one time window on treatment, the worst value will be selected for the by-visit analyses.

7. PLANNED ANALYSIS

For End-Of-Text (EoT) tables, the set of summary statistics includes: N / Mean / SD / Min / Q1 (lower quartile) / Median / Q3 (upper quartile) / Max.

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 patients in the respective patient set whether they have non-missing values or not).

Percentages will be rounded to one decimal place. The category missing will be displayed only if there are actually missing values.

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.

7.3 TREATMENT COMPLIANCE

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

Compliance will be calculated for subjects having attended the visit. A subject is considered having attended the visit if the indicated visit is captured in the eCRF database. In particular, if a subject attended the visit, but is not treated at the visit, the compliance of this visit is considered as 0%.

Compliance with trial medication will be based on the drug infusion/administered eCRF data and calculated as amount of drug infused/administered divided by the amount of drug to be infused/administered expressed as a percentage, see calculations below.

"Per Visit" compliance to trial medication will be calculated as follows:

$$\frac{(\text{Amount of drug infused/administered at Visit X(n)})}{(\text{Amount of drug planned to be infused/administered at Visit X(n)})} \times 100$$

Overall compliance for first treatment cycle of all patients will be calculated as mean of "per visit" compliance at visit Day 1.

Overall compliance for second treatment cycle onwards (from Day 22 onwards) of all patients will be calculated as mean of "per visit" compliance at each visit. Overall compliance to trial medication will be calculated as mean of the "per visit" compliance.

The compliance will be based on the total volume infused in mL (eCRF data) compared to total volume prepared (eCRF data).

7.4 PRIMARY ENDPOINT(S)

The analysis of primary endpoints will be performed as defined in the CTP with the approach proposed by Berry et al. (2013). Posterior distributions for the ORRs will be summarized with Mean, Median, 2.5%, and 97.5 % quantiles.

7.5 SECONDARY ENDPOINT(S)

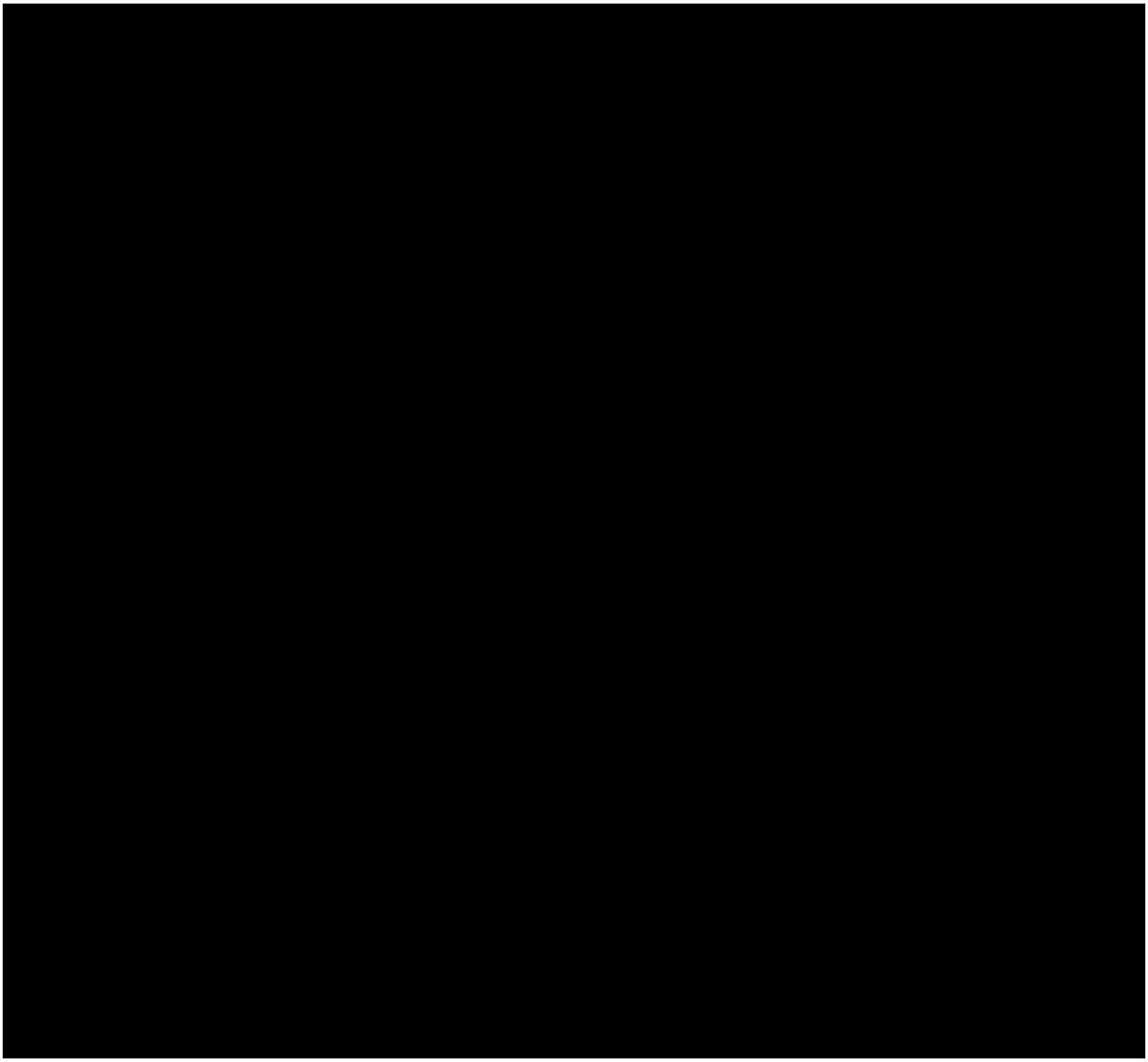
The analysis of secondary endpoints will be performed as defined in the CTP.

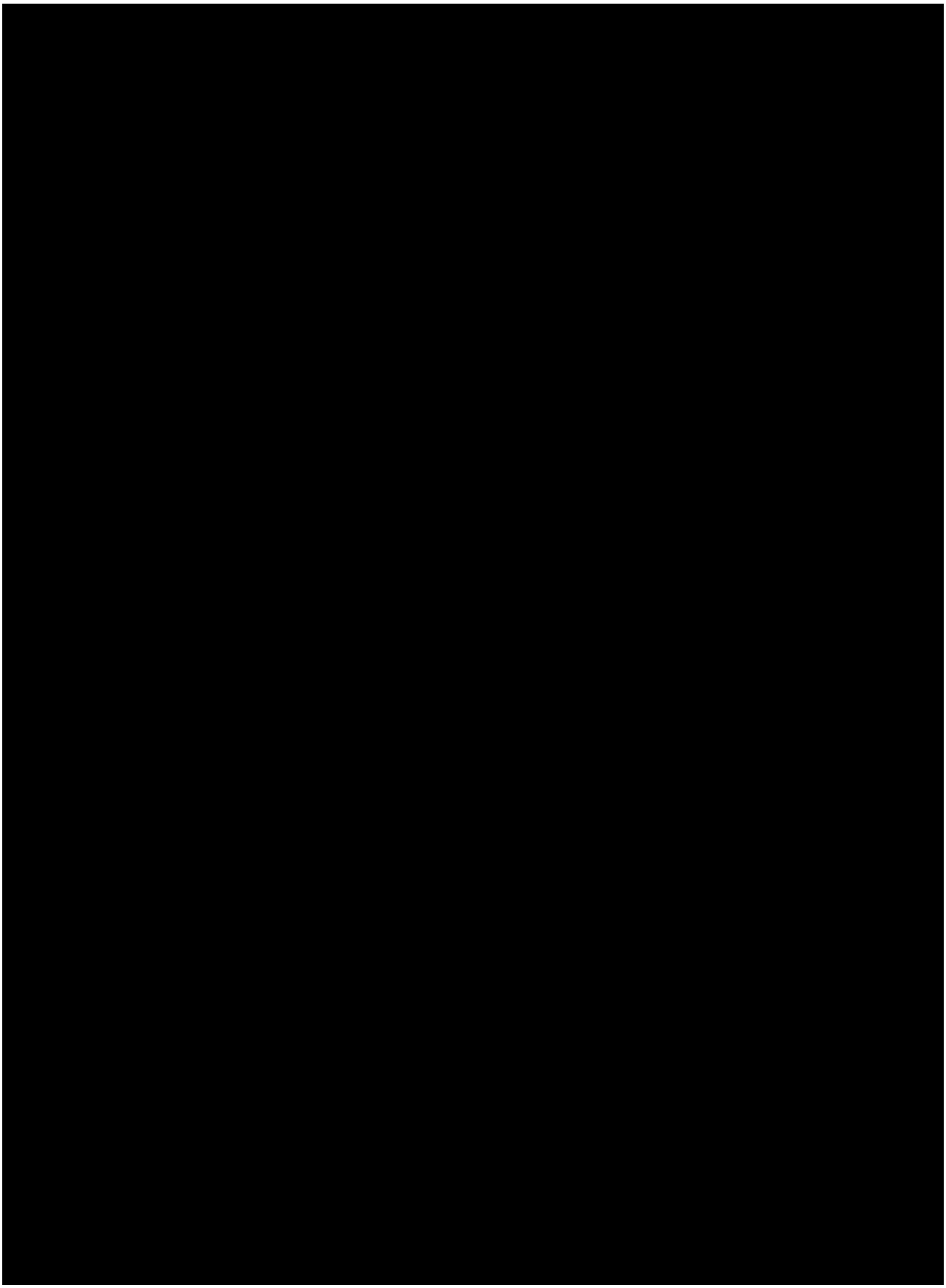
7.5.1 Key secondary endpoint(s)

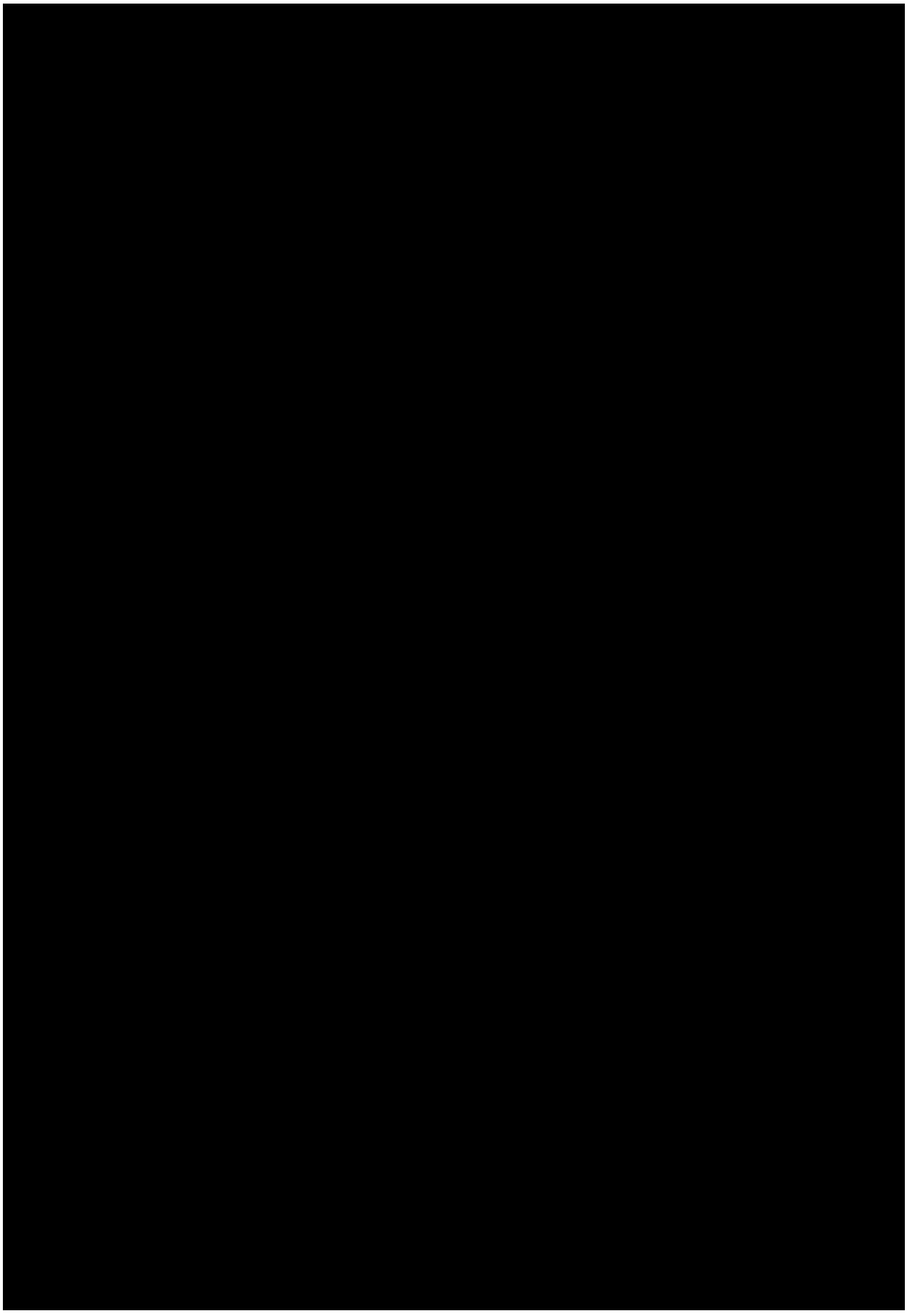
This section is not applicable as no key secondary endpoint has been specified in the protocol.

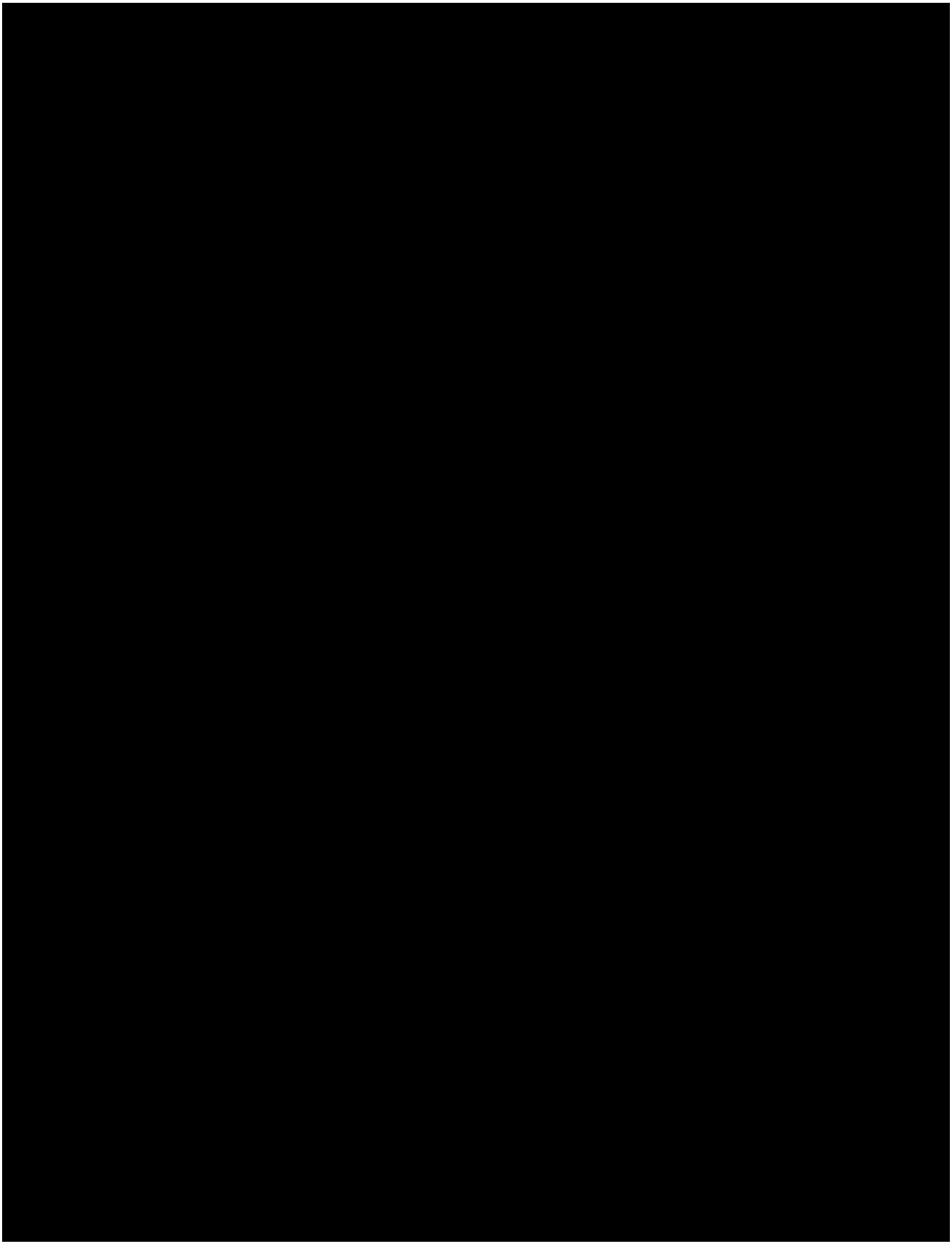
7.5.2 (Other) Secondary endpoint(s)

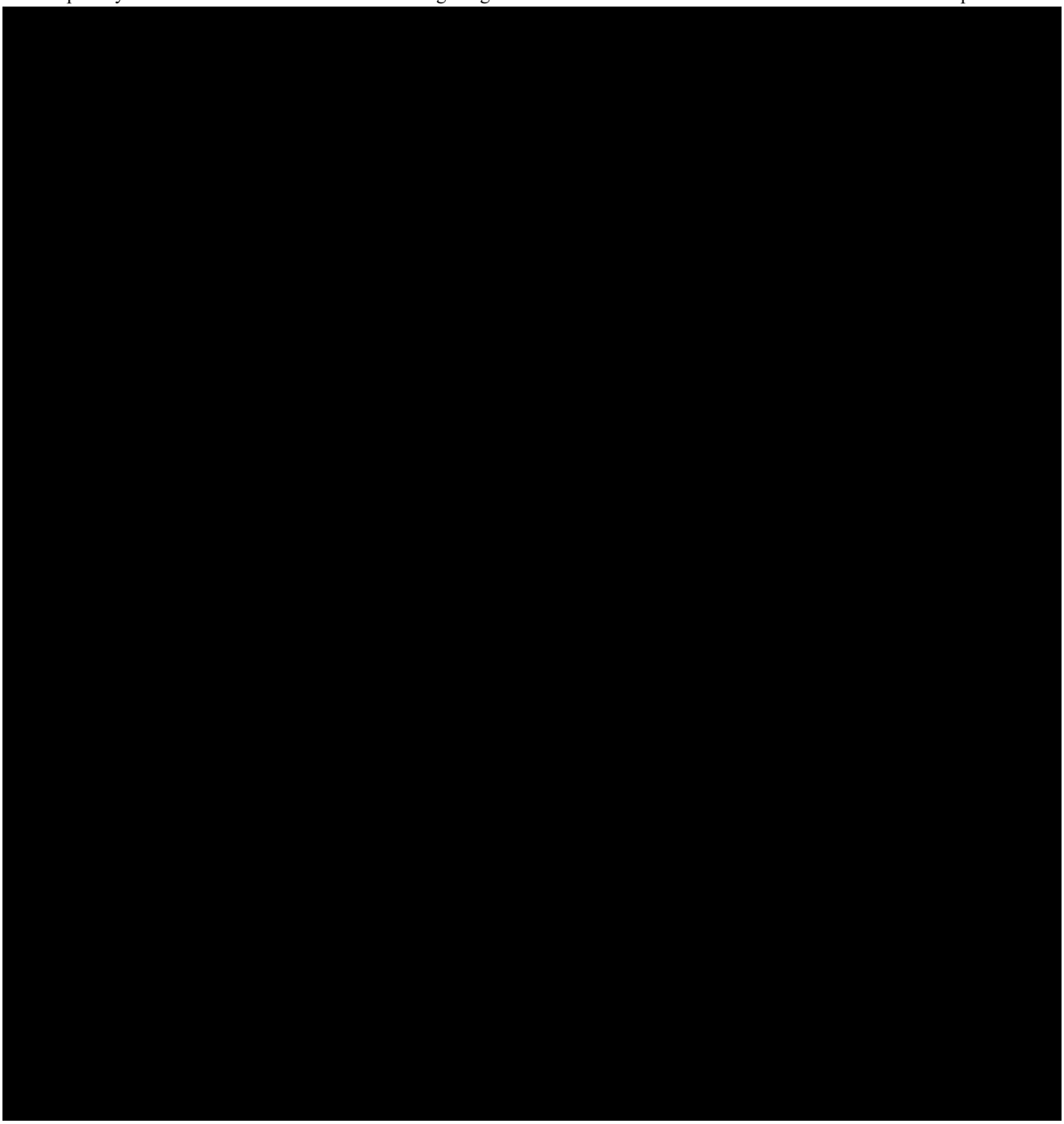
Not applicable.











7.7 EXTENT OF EXPOSURE

Treatment exposure will be primarily summarized by the total on-treatment time and has been defined in Section 5.4 of this TSAP.

Treatment interruptions before permanent discontinuation will not be excluded. In Part 1, summary statistics for treatment time by each dose level and the dosage of BI 836880 over time will also be provided.

7.8 SAFETY ANALYSIS

The safety analyses will be performed as defined in the CTP. All safety analyses will be performed on the treated set of Part 1 and Part 2 of this trial.

7.8.1 Adverse events

The analyses of adverse events (AE) will be descriptive in nature. All analyses of AEs will be based on the number of patients with AEs and not on the number of AEs. Two analyses will be performed. The first analysis of safety will be performed for the first part of the trial (determination of the MTD/RP2D, first cycle only, dose level = initial dose at the start of the treatment, treated set). This descriptive analysis will evaluate the MTD/RP2D. The second analysis will be performed with respect to all cycles for part 1 and will act as a support for the determination of the MTD/RP2D (treated set).

For analysis of duration, severity, etc. of multiple AE occurrences, data on the case report form (CRF) will be collapsed into AE episodes provided that all of the following applies:

- The same MedDRA lowest level term was reported for the occurrences.
- The occurrences were time-overlapping or time-adjacent (time-adjacency of two occurrences is given if the second occurrence started on the same day or on the day after the end of the first occurrence).
- Treatment did not change between the onset of the occurrences or treatment changed between the onsets of the occurrences, but no deterioration was observed for the later occurrence.

For further details on summarization of AE data, please refer to the guideline 'Handling and summarization of adverse event data for clinical trial reports and integrated summaries' (5).

For patients treated with the test drug, that means that all adverse events occurring between first drug infusion and the REP after last drug infusion or death, whichever occurs first, will be assigned to the on-treatment period. All adverse events occurring before any study drug infusion will be assigned to ‘screening’ and all adverse events occurring after last study drug infusion + the REP will be assigned to ‘post-study’ (for listings only). For details on the treatment definition, see Section 6.1.

An overall summary of adverse events will be presented. This summary will exclude the rows ‘Severe AEs’, ‘Significant AEs’ and ‘Other significant AEs’ but will include additional rows for ‘AEs leading to dose reduction’, ‘AEs leading to death’ and ‘AEs by highest Common Terminology Criteria (CTC) grade’.

Additional AE tables will be produced for AEs of special interest (hepatic injury as defined in CTP Section 5.2.7.1 and DLTs as defined in CTP Section 5.2.6.1), providing further details on highest CTC grade, action taken with study drug, and time to first onset of AE.

The frequency of patients with adverse events will be summarized by maximum CTC grade (grades 1, 2, 3, 4, 5 and all grades), treatment, primary system organ class and preferred term for each of the following AE tables as well as relatedness of AEs to treatment and seriousness:

- All AEs

- Drug-related AEs
- Immune-related AEs
- AEs leading to dose reduction
- Drug-related AE leading to dose reduction
- Immune-related AEs leading to dose reduction
- AEs leading to treatment discontinuation
- Drug-related AEs leading to treatment discontinuation
- Immune-related AEs leading to treatment discontinuation
- Drug-related AEs leading to treatment discontinuation or dose reduction
- Immune-related AEs leading to treatment discontinuation or dose reduction
- AEs leading to death
- Serious AEs
- Drug-related serious AEs
- AESIs
- DLTs (in Part 1 dose escalation only)

All tables will be sorted by system organ class (SOC) according to the standard sort order specified by the European Medicines Agency (EMA). Preferred terms (PTs) will be sorted by frequency (within SOC).

The above tables will be repeated with the project-defined grouping of AE terms. Details of the project-defined groupings are defined in the technical TSAP. In these tables, the grouped AEs will replace the original PTs for all AEs that are included within the grouped term. The grouped AE categories will then be tabulated along with all remaining MedDRA PTs, sorted by descending frequency.

A reference table presenting the entire project defined groupings and MedDRA PTs within each grouping will also be produced.

The frequency of patients with user defined AEs will be presented by special search category, preferred term, and highest CTCAE grade. Special search categories (SSCs) for AEs are defined in Table 7.8.1: 1 below.

Table 7.8.1: 1 Definitions of SSCs

N	Medical concept	Definition (for programmers)	Other monitoring options
1	Fatigue / asthenia	HLT 10003550	
2	Hypertension	SMQ 20000147	Narrow
3	Proteinuria	SMQ 20000220	Narrow
4	Haemorrhage	SMQ 20000040 SMQ 20000039	Narrow Narrow
5	Embolic and thrombotic events	SMQ 20000081 SMQ 20000115	Narrow Narrow and broad
6	GI perforation	SMQ 20000107	Narrow

N	Medical concept	Definition (for programmers)	Other monitoring options
7	Infusion related reactions	SMQ 20000021 + PT 10051792 + PT 10082742	Narrow
8	Cardiac failure	SMQ 20000004	Narrow and broad

Additional SSCs for AEs that are to be completed for combination studies with ezabenlimab (BI 754091) are defined in Table 7.8.1: 2 below.

Table 7.8.1: 2 Definitions of SSCs from combination studies with ezabenlimab (BI 754091)

N	Term	Definition#	SMQ code
1	Non-infectious diarrhoea	Noninfectious diarrhea (SMQ) Broad	20000218
2	Drug related hepatic disorders	Drug related hepatic disorders - comprehensive search (SMQ) Broad	20000005
3	ILD	Interstitial lung disease (SMQ) Narrow	20000042
4	Thyroid dysfunction	Thyroid dysfunction (SMQ) Broad	20000159
5	SCAR	Severe cutaneous adverse reactions (SMQ) Broad	20000020
6	Peripheral neuropathy	Peripheral neuropathy (SMQ) Broad	20000034
7	Non-infectious meningitis	Noninfectious meningitis (SMQ) Broad	20000134
8	Non-infectious encephalitis	Noninfectious encephalitis (SMQ) Broad	20000132
9	Acute renal failure	Acute renal failure (SMQ) Broad	20000003
10	Cardiomyopathy	Cardiomyopathy (SMQ) Broad	20000150
11	Guillain-Barre syndrome	Guillain-Barre syndrome (SMQ) Broad	20000131
12	Haematopoietic cytopenias	Haematopoietic cytopenias (SMQ) Broad	20000027
13	Acute pancreatitis	Acute pancreatitis (SMQ) Broad	20000022
14	Cardiac arrhythmias	Cardiac arrhythmias (SMQ) Broad	20000049
15	Heart failure	Cardiac failure (SMQ) Narrow	20000004
16	Vasculitis	Vasculitis (SMQ) Narrow	20000174

This column indicates whether the Term(s) provided in the first column are MedDRA preferred terms (PT), Standardised MedDRA Queries (SMQ), or BI customized MedDRA Queries (BIcMQ).

7.8.2 Laboratory data

The analyses of laboratory data will be descriptive in nature and will be based on BI standards "Display and Analysis of Laboratory Data" (7). CTC grade for applicable lab parameters will be calculated according to CTCAE v5.0 (6).

Descriptive statistics of all converted laboratory values by visit will be provided including changes from baseline. Frequency tables of transitions relative to the reference range and of possible clinically significant abnormalities will be produced. For those parameters that have CTC grading possible clinically significant abnormalities are defined as those laboratory values with a CTC grade ≥ 2 that have had an increase of ≥ 1 grade from baseline. For those parameters for which no CTC grade has been defined standard BI project definitions will be used to decide on clinical significance. Further frequency table will show the transition of CTC grade from baseline to worst value and from baseline to last value on treatment.

Summaries will be produced of laboratory data recorded prior to treatment, on-treatment and post-treatment. For details on the treatment definition, see Section 6.1.

The focus of the laboratory data analysis will be on the following laboratory parameters:

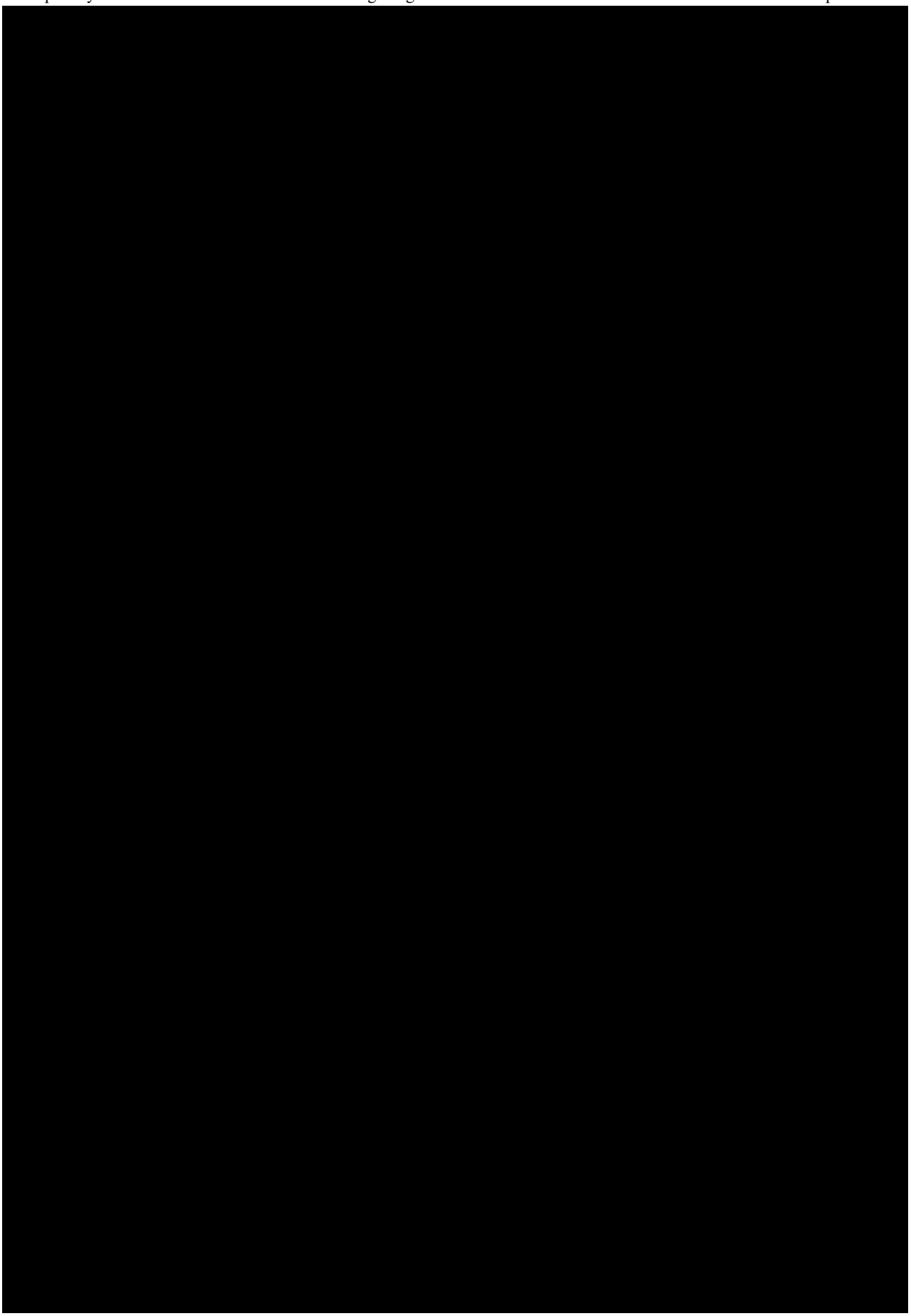
- Low values: Activated Partial Thromboplastin Time (aPTT), Prothrombin Time (PT), International Normalised Ratio (INR), White Blood Cell Count (WBC) with differential, Platelets (PLT)
- High values: Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), bilirubin, Alkaline Phosphatase (AP), Activated Partial Thromboplastin Time (aPTT), Prothrombin Time (PT), International Normalised Ratio (INR), Protein levels in urine

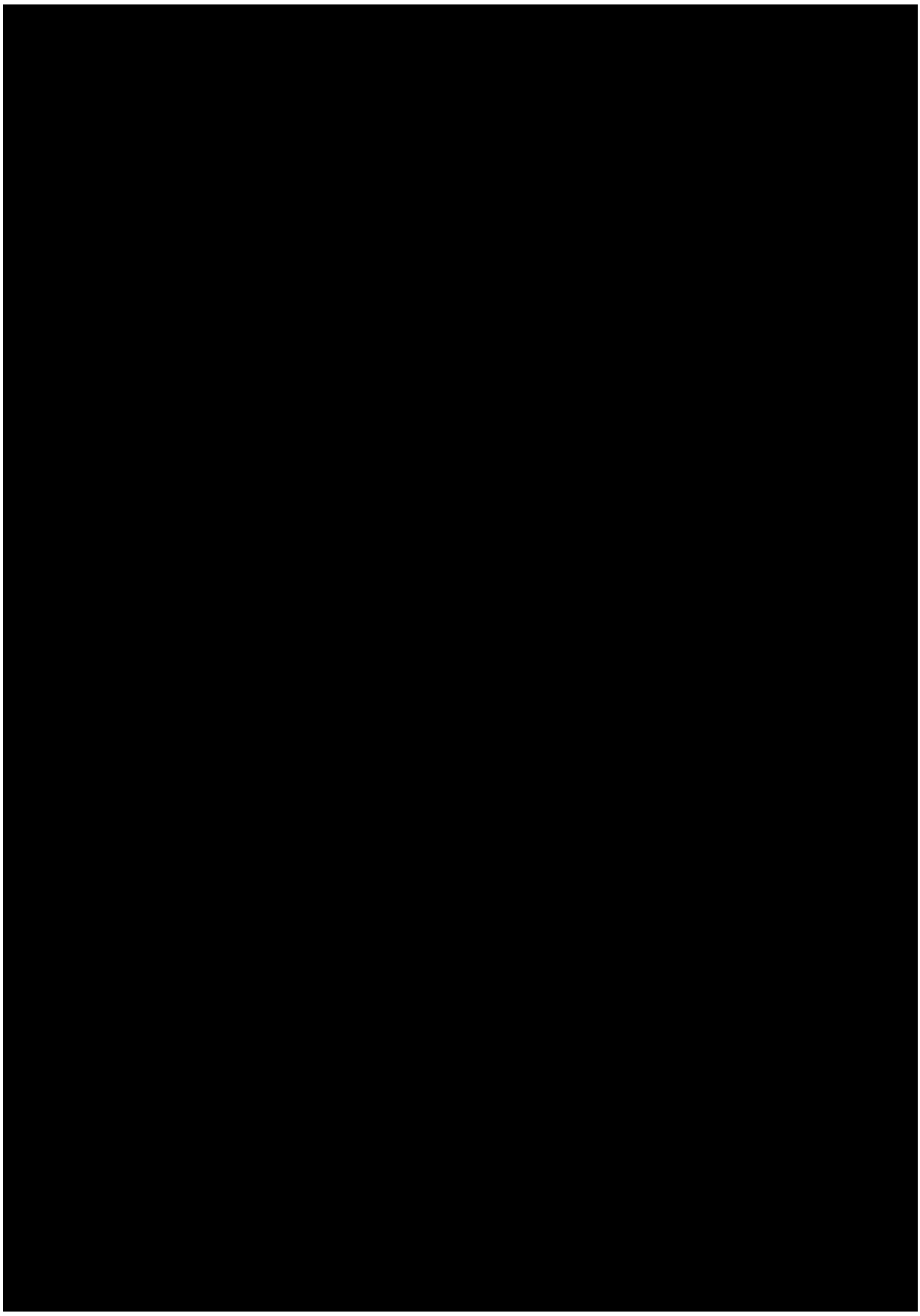
7.8.3 Vital signs

Only descriptive statistics are planned for this section of the report. A shift table will be provided for change from baseline over the course of treatment for systolic and diastolic blood pressure.

7.8.4 ECG

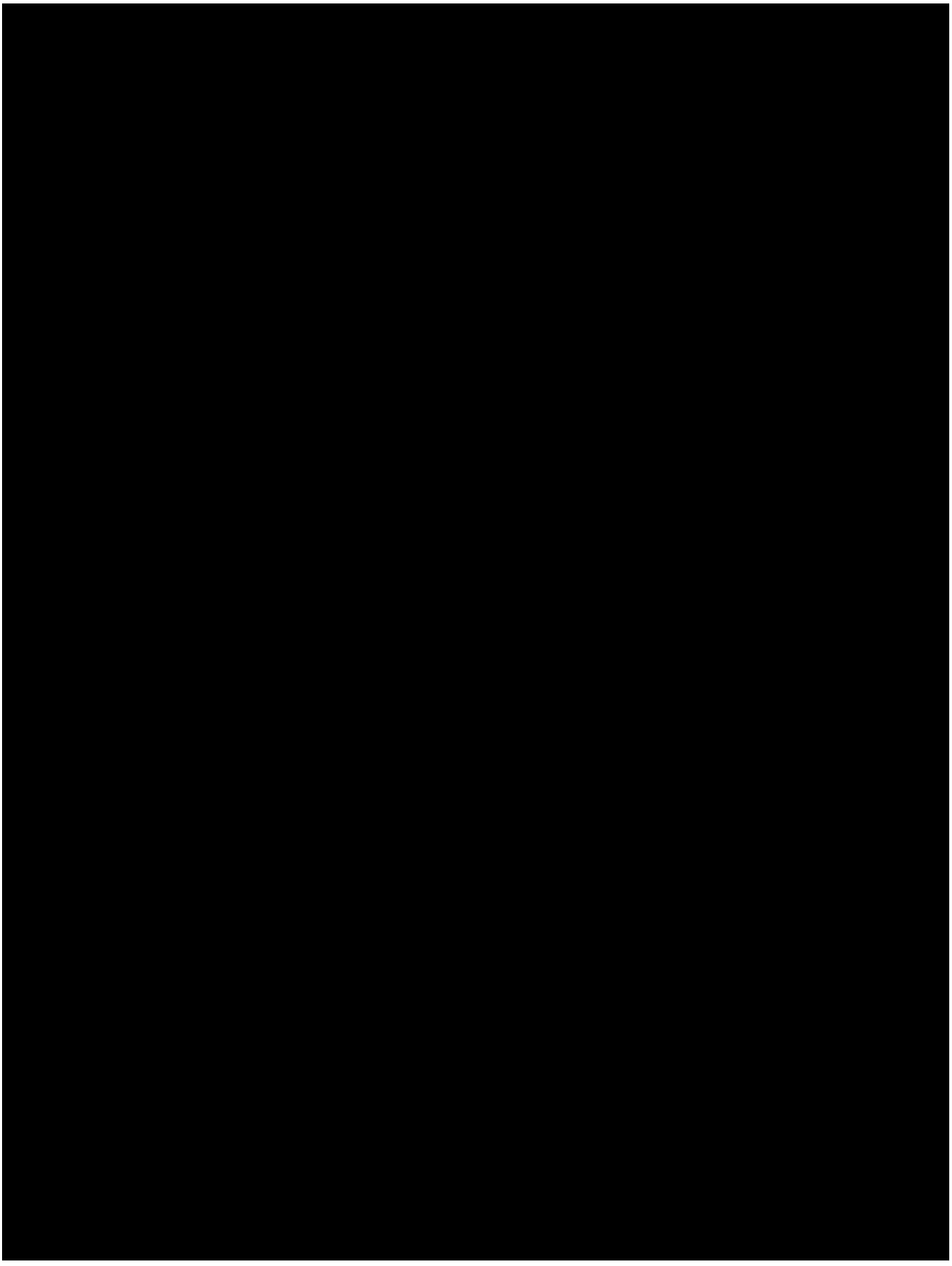
ECG data will be collected as described in CTP Section 5.2.4. Clinically significant findings in ECG data will be reported under "Adverse events" if applicable and will be analysed accordingly. In addition, patients with abnormal overall assessments at any time on treatment will be summarized in a descriptive manner.

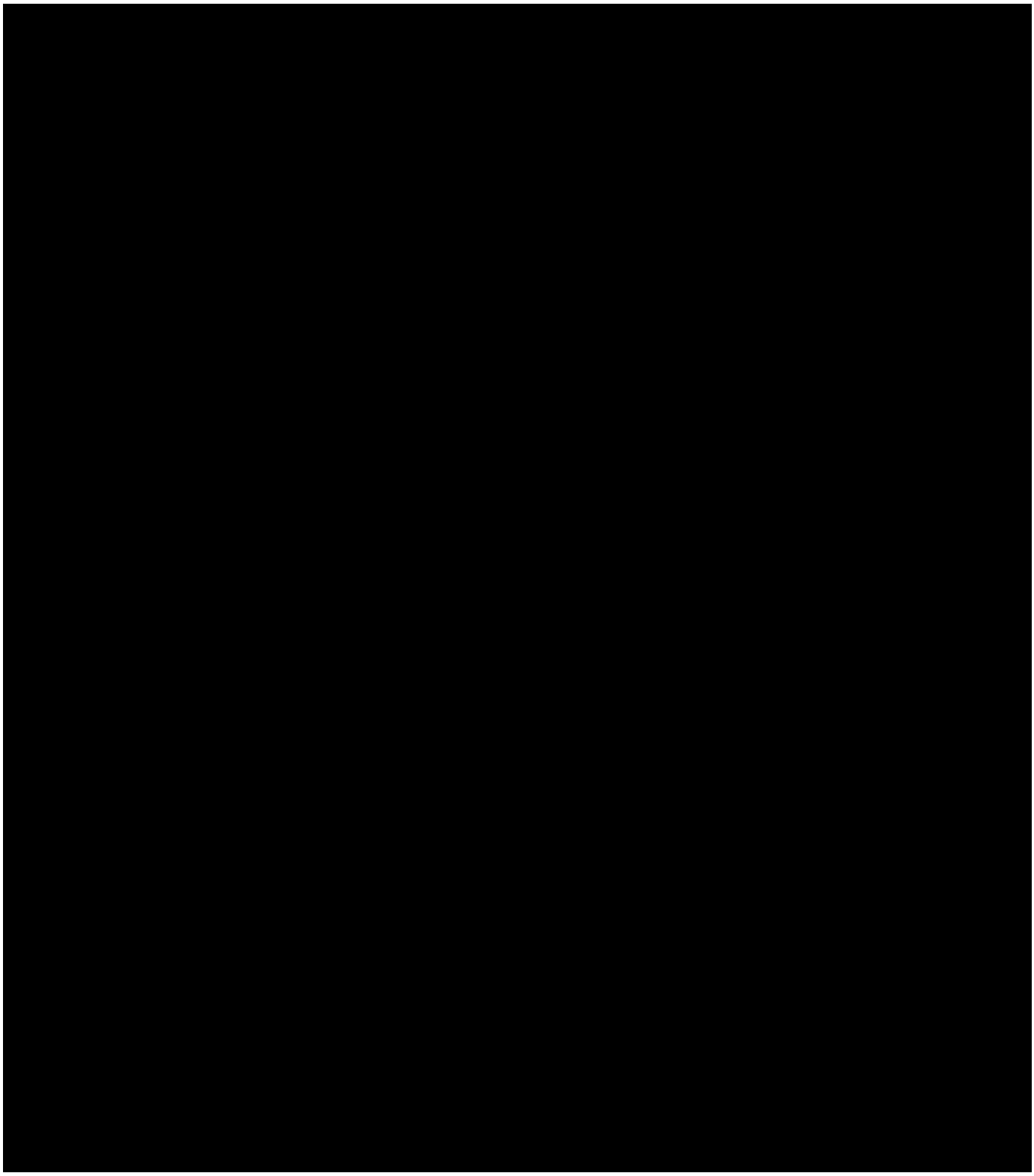




8. REFERENCES

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	*001-MCS 36-472: "Standards and processes for analyses performed within Clinical Pharmacokinetics/Pharmacodynamics", current version; IDEA for CON.*
3	*001-MCG-156_RD-01: "Handling of missing and incomplete AE dates", current version; IDEA for CON.*
4	*001-MCG-420: "Statistical Methods for Pharmacokinetics", Version 3.0, IDEA for CON.*
5	*001-MCG-156: "Handling and summarization of adverse event data for clinical trial reports and integrated summaries", current version; IDEA for CON.*
6	*Common Terminology Criteria for Adverse Events (CTCAE): version 5.0, published: November 27, 2017 (v5.0) https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf (access date: April 14, 2020), U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute 2017.*
7	*001-MCG-157: "Handling, Display and Analysis of Laboratory Data", current version; IDEA for CON.*





10. HISTORY TABLE

Table 10: 1 History table

This is a revised TSAP including the following modifications.

Version	Date (DD-MMM-YY)	Author	Sections changed	Brief description of change
Initial	**18-APR-2018**	[redacted]	None	This is the initial TSAP with necessary information for trial conduct.
Revised	**17-APR-2020**		Sections 2, 5, 6, 7, 8	This is a revised TSAP with revisions reflecting changes in CTP version 5.0.
Revised	**26-OCT-2020**		[redacted]	
Revised	**19-MAR-2021**			

Version	Date (DD-MMM-YY)	Author	Sections changed	Brief description of change
Revised	**23-AUG-2021**	[redacted]	[redacted]	[redacted]
Revised	**05-MAY-2022**			
Final	***DD-MMM-YY***	*XX*	*XX*	*This is the final TSAP.*

APPROVAL / SIGNATURE PAGE

Document Number: c23146709 **Technical Version Number:3.0**

Document Name: 8-01-tsap

Title: An open label phase Ib dose finding study of BI 836880 in combination with ezabenlimab to characterize safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy in patients with locally advanced or metastatic non-squamous Non-Small Cell Lung Cancer and in other solid tumors

Signatures (obtained electronically)

Meaning of Signature	Signed by	Date Signed
Approval-Team Member Medicine	[redacted]	28 Jun 2022 22:30 CEST
Approval-Clinical Trial Leader		29 Jun 2022 08:21 CEST
Approval-Medical Writer		29 Jun 2022 11:42 CEST
Approval-Project Statistician		29 Jun 2022 14:33 CEST
Approval-Translational Medicine Expert		30 Jun 2022 04:15 CEST
Approval-Clinical Pharmacokinetics		30 Jun 2022 16:36 CEST

(Continued) Signatures (obtained electronically)

Meaning of Signature	Signed by	Date Signed