TRIAL STATISTICAL ANALYSIS PLAN

c27797453-01

BI Trial No.:	1199.324
Title:	Study of Pulmonary Rehabilitation In Nintedanib Treated Patients with IPF: Improvements in Activity, Exercise Endurance Time, and QoL
Investigational Product(s):	Nintedanib
Responsible trial statistician(s):	[redacted]
Date of statistical analysis plan:	18 SEP 2020
Version:	Final

Page 1 of 25

1. TABLE OF CONTENTS

TITLE PAGE....1
1. TABLE OF CONTENTS....2
2. LIST OF ABBREVIATIONS....4
3. INTRODUCTION....4
4. CHANGES IN THE PLANNED ANALYSIS OF THE STUDY....5
5. ENDPOINTS....5
5.1 PRIMARY ENDPOINT....5
5.2 SECONDARY ENDPOINTS....5
5.2.1 Key secondary endpoints....5
5.2.2 Secondary endpoints....5
[redacted]
6. GENERAL ANALYSIS DEFINITIONS....9
6.1 TREATMENT(S)....9
6.2 IMPORTANT PROTOCOL DEVIATIONS....10
6.3 SUBJECT SETS ANALYSED....11
[redacted]
6.5 POOLING OF CENTRES....11
6.6 HANDLING OF MISSING DATA AND OUTLIERS....11
6.7 BASELINE, TIME WINDOWS AND CALCULATED VISITS....12
7. PLANNED ANALYSIS....14
7.1 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS....14
7.2 CONCOMITANT DISEASES AND MEDICATION....14
7.3 TREATMENT COMPLIANCE....15
7.4 PRIMARY ENDPOINT....15
7.4.1 Primary analysis of the primary endpoint....15
7.4.2 Sensitivity analysis of the primary endpoint....15
7.5 SECONDARY ENDPOINTS....16
7.5.1 Key secondary endpoint....16
7.5.2 (Other) Secondary endpoints....16
[redacted]
7.7 EXTENT OF EXPOSURE....19
7.8 SAFETY ANALYSIS....19
7.8.1 Adverse Events....19
7.8.2 Laboratory data....20
7.8.3 Vital signs....20
7.8.4 ECG....20
7.8.5 Others....20
8. REFERENCES....21
[redacted]
10. HISTORY TABLE....25

LIST OF TABLES

Table 6.2: 1 Important protocol deviations.....10
Table 10: 1 History table 25

2. LIST OF ABBREVIATIONS

See Medicine Glossary:
http://glossary

Term	Definition / description
6MWT	Six-Minute Walk Test
DLco	Carbon Monoxide Diffusion Capacity
DM&SM	Boehringer Ingelheim Data Management and Statistics Manual
FVC	Forced Vital Capacity
IPD	Important Protocol Deviation
KBILD	King's Brief ILD Questionnaire
MMRM	Mixed effect Model for Repeated Measures
Q1	Lower quartile
Q3	Upper quartile
QoL	Quality of Life
SD	Standard deviation
SGRQ	St. George's Respiratory Questionnaire
SOC	System organ class
SpO_2	Oxygen Saturation on Pulse Oximetry
UCSD-SOBQ	University of California, San Diego Shortness-of-Breath Questionnaire

3. INTRODUCTION

As per International Conference on Harmonisation (ICH) E9, 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."

SAS® Version 9.4 will be used for all analyses.

4. CHANGES IN THE PLANNED ANALYSIS OF THE STUDY

In writing the core TSAP, these corrections were made to the specifications of the initial TSAP:

1. Important protocol deviation (IPD) E1 in Section 6.2 "No post-baseline 6 MWT assessments" was clarified to E1 "No post-baseline 6 MWD assessments at 12 weeks" and E2 "No baseline 6 MWD assessments" to reflect the primary outcome being measured at 12 week visit.
2. iPD D2 in Section 6.2 was changed from "Discontinued nintedanib" to "Discontinued nintedanib before 12 week visit" to reflect the primary outcome being measured at 12 week visit.
3. The Screening trial period in Section 6.1 was changed from "informed consent to randomization" to "first informed consent to randomization" to account for re-consenting of patients.
4. The trial periods defined in Section 6.1 was clarified to make the distinction between efficacy analysis and safety analysis.

Following termination of the trial, limited efficacy analysis will be performed for an abbreviated CTR. Primary and secondary endpoints will be limited to descriptive outcome measures. Further endpoints will not be done.

5. ENDPOINTS

5.1 PRIMARY ENDPOINT

The primary endpoint is the change from baseline in Six-Minute Walk Test (6MWT) distance at 12 weeks.

5.2 SECONDARY ENDPOINTS

5.2.1 Key secondary endpoints

There are no key secondary endpoints defined for this trial.

5.2.2 Secondary endpoints

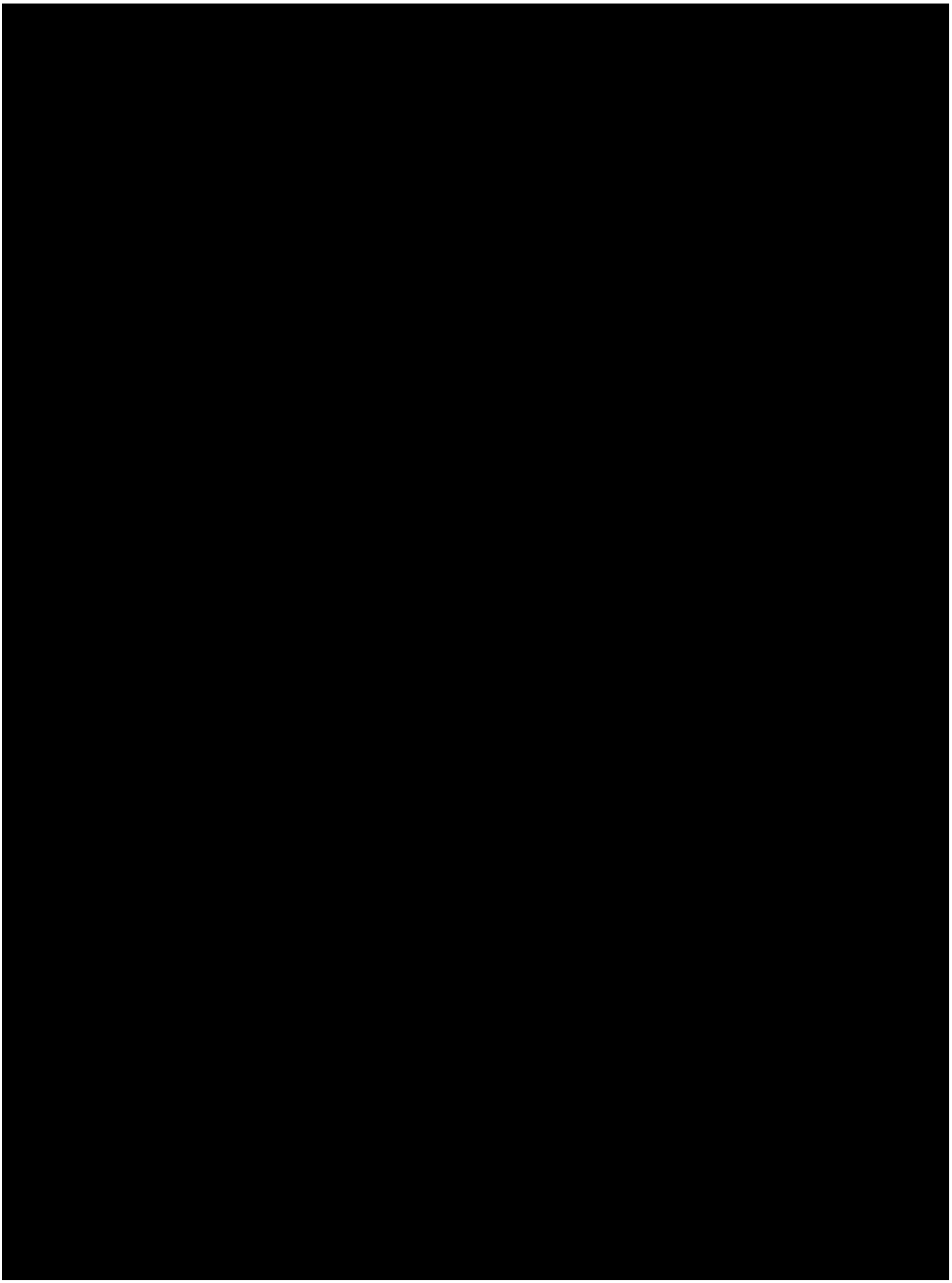
The secondary endpoints are:

- Change from baseline in Quality of Life (QoL) (SGRQ, KBILD, UCSD-SOBQ) at 12 and 24 weeks
- Change from baseline in 6MWT distance at 24 weeks
- Change from baseline in Forced Vital Capacity (FVC) at 12 weeks and 24 weeks using each of
    - Absolute change from baseline of FVC and FVC % predicted
    - Relative change from baseline of FVC and FVC % predicted
    - Absolute categorical change of FVC % predicted (decrease by >5%, increase by >5%, and change within ≤ 5%)

  - Absolute categorical change of FVC% predicted (decrease by >10%, increase by >10%, and change within ≤ 10%)
- Change from baseline in daily accelerometer activity from baseline at 12 and 24 weeks
  - Score of average Steps/day
  - Score of average VMU/day

Refer to Section 6.7 for baseline value definition. Refer to Section 6.6 for missing baseline assessment.

[redacted]



6. GENERAL ANALYSIS DEFINITIONS

6.1 TREATMENT(S)

For treatment specifications, see Section 4 of the CTP.

The following trial periods will be defined with respect to efficacy analyses: Screening, Post-randomization, Treatment, Post-treatment.

- Screening: from first informed consent to randomization
- Post-randomization: from randomization to day of first pulmonary rehabilitation (for those randomized to Pulmonary Rehabilitation Treatment group)
- Treatment:
    - For patients randomized to the Non-Pulmonary Rehabilitation Treatment group: from randomization to the visit 7 end-of-trial visit
    - For patients randomized to the Pulmonary Rehabilitation Treatment group: from first day of pulmonary rehabilitation to the visit 7 end-of-trial visit
- Post-treatment: after the visit 7 end-of-trial visit

Efficacy analyses is independent of nintedanib usage: any dose interruption or discontinuation has no effect on the efficacy analyses. Efficacy analyses will be done on the Post-randomization and Treatment Periods.

The following trial periods will be defined with respect to safety analyses:

Note: the last day of each of the following periods is excluded.

- Screening: from first informed consent to randomization
- Post-randomization: from randomization to day of first Nintedanib drug intake on/after randomization. This period only exists if Nintedanib first drug intake on/after randomization occurred at least 1 day after randomization.
- Treatment: from first Nintedanib drug intake on/after randomization (or re-start of nintedanib if interruption) to last Nintedanib drug intake (or the day before start date of interruption if interruption) plus one day.
- Off-treatment [a]: From the start date of Nintedanib interruption to re-start of Nintedanib treatment.
- Residual-effect [a]: From the last Nintedanib drug intake plus one day to last Nintedanib trial drug intake plus 28 days plus one day.
- Post-treatment [a]: From last trial drug intake plus 29 days. Note, this period is only created if last Nintedanib intake plus 29 days took place before trial completion.
- Post-study: from the latest of last trial drug intake plus 29 days or date of trial completion plus 1 day

[a] Note: This period is optional insofar as it does not necessarily exist for all patients.

6.2 IMPORTANT PROTOCOL DEVIATIONS

The following table defines the different categories of important protocol deviations (IPD) to be considered. Important efficacy IPDs are those that can potentially influence the primary endpoint. No patients will be excluded from the analyses based on those IPDs as no per-protocol analysis is planned. However, the frequency of patients with IPDs will be presented.

Table 6.2: 1 Important protocol deviations

Category / Code		Description	Requirements
A		**Entrance criteria not met**	
	A1	Inclusion criteria not met	Inclusion criteria not met as specified in the protocol. *Automatic PD*
	A2	Exclusion criteria not met	Exclusion criteria not met as specified in the protocol. *Automatic PD*
B		**Informed consent**	
	B1	Informed consent not available/not done	Informed consent date missing *Automatic PD*
	B2	Informed consent too late	CRF date of informed consent *Automatic PD*
	B3	Informed re-consent not available/not done	Informed re-consent date missing *Manual PD*
	B4	Informed re-consent too late	CRF date of informed re-consent *Manual PD*
	B5	Incorrect consent form used or other consenting process error	*Manual PD*
C		**Trial treatment and randomisation**	
	C1	Incorrect treatment given	Patient assigned to pulmonary rehabilitation not prescribed rehab, or patient assigned to standard care prescribed rehab *Manual PD with medical review of MQRM listings*
	C2	Non-compliance	Pulmonary Rehabilitation Compliance <80% or >120% *Automatic PD with medical review of MQRM listings*
D		**Concomitant medication**	
	D1	Patient received prohibited concomitant therapies during treatment phase	*Manual PD with medical review of MQRM listings*
	D2	Mandatory medication not taken	Discontinued nintedanib before 12 week visit *Automatic PD*
E		**Missing data**	
	E1	No post-baseline 6 MWD assessments at 12 weeks	*Automatic PD*
	E2	No baseline 6 MWD assessments	*Automatic PD*

Automatic PDs are those detected via an automatic programming process using SAS. Manual PDs are those identified during the MQRM meeting through patient listings and/or BI CTMS.

6.3 SUBJECT SETS ANALYSED

- Screened set
  This patient set includes all patients having signed informed consent and performed visit 1.
- Randomized set (RS)
  This patient set includes all randomized patients, whether treated with pulmonary rehabilitation or not
- [redacted]

All analyses will be done on the RS or [redacted]. Note that the number of patients with available data for an endpoint may differ. For details, see Section 6.6.

[redacted]

6.5 POOLING OF CENTRES

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

6.6 HANDLING OF MISSING DATA AND OUTLIERS

In general, the efficacy analyses as well as safety analyses will be evaluated by observed case analysis (OC), i.e. using only available data without imputation.

6.6.1 Primary Endpoint

~~Multiple imputation will be used to handle missing data as a sensitivity analysis for the primary endpoint. Further detail is provided in Section 7.4.2.~~

6.6.2 Secondary Endpoints

6.6.2.1 Saint George's Respiratory Questionnaire

For the SGRQ, the SGRQ manual (7) allows for 25% of missing data per component (i.e., 2

questions for symptoms, 6 questions for impacts and 4 questions for activities). The rules defined in the SGRQ manual will be used to derive the SGRQ.

Additionally the responses to questions 5 and 6 (see CTP Section 10.3 for questionnaire) will be made consistent to the extent that if the answer to question 5 is 5 (none of the time) and the answer to question 6 is non-missing (i.e., length of worst attack specified), then question 6 will be set to missing. Therefore scores will be calculated ignoring that item. In this case, the missing response to question 6 will not be included in the count of missing questions for the symptoms component.

6.6.2.2 University of California, San Diego Shortness-of-Breath Questionnaire

If UCSD-SOBQ is not completely answered, the missing questions will not be imputed and the score will be set to missing.

6.6.2.3 King's Brief ILD Questionnaire

For K-BILD, missing item scores are imputed based on the average of the non-missing item scores within the domain, rounded to the nearest integer. If the missing items are >50% per domain, then the domain score is set to missing. If item 15 is missing, it will be replaced by the average of all available items 1-14. If any of the domain scores are missing, the total score is set to missing.

6.6.3 Other Endpoints

6.6.3.1 Concomitant therapies

In case of (partially) missing start and end dates of concomitant therapies, the dates will be imputed so that the extent of exposure to the concomitant therapy is maximal, i.e. the first day (month) of the month (year) for incomplete start dates and the last day (month) of the month (year) for incomplete end dates.

6.6.3.2 Safety Endpoints

Information regarding acute IPF exacerbations is collected from AEs and as such, missing or incomplete start or end dates will be imputed according to BI standards (1).

6.7 BASELINE, TIME WINDOWS AND CALCULATED VISITS

As a general rule, last assessment before treatment period start (included) will be used as baseline. For patients randomized to the Non-Pulmonary Rehabilitation group treatment period starts from randomization. For patients randomized to the Pulmonary Rehabilitation group treatment period starts from first day of pulmonary rehabilitation. If the baseline value is missing and the screening value is available, then the baseline value will be defined as the screening value taken closest to baseline date.

A windowing will be performed in order to assign data to the relevant study visit based on the actual day of the assessment. If after windowing of visits at baseline, two values fall within the same baseline interval, then the last value will be taken into account. If after windowing of

post-baseline visits, two visits fall in the same interval, then the measurement closest to the planned visit will be taken into account. In case two measurements are equidistant from the planned visit, then the last one will be picked.

Time windowing rules for physical exam, vital signs, and laboratory tests:

Time window of actual day			Allocated to		
Start day	End day (included)	Length of the time-window [days]	Visit number	Visit name	Planned day of the visit
-	1	-	2	Baseline	1
2	32	31	3	3 weeks	22
33	63	31	4	6 weeks	43
64	105	42	5	12 weeks	85
106	147	42	6	18 weeks	127
148	-	-	7	24 weeks	169

Time windowing rules for spirometry, six minutes walk test, [redacted], PROactive tool, SGRQ, KBILD, UCSD SOBQ:

Time window of actual day			Allocated to		
Start day	End day (included)	Length of the time-window [days]	Visit number	Visit name	Planned day of the visit
-	1	-	2	Baseline	1
2	126	125	5	12 weeks	85
127	-	-	7	24 weeks	169

Include for analysis and in average calculation of the ProActive tool scores the following measurements. If a patient does not have at least 5 days of measurements available, no score is calculated (except for baseline, noted below).

- Baseline = 7 days before and up to actual Visit 2 (excluded). If a patient does not have at least 5 days of measurements within this time window, then use 7 days before and up to actual Visit 1 (excluded) (only if 5 days of measurements are available)
- 12 weeks = 7 days before and up to actual Visit 5 (excluded)
- 24 weeks = 7 days before and up to actual Visit 12 (excluded)

Note: For accelerometer scores, if a patient has more than one record for a given day, the record will not be used for calculation. For eDiary scores, if a patient has more than one record for a given day, the worse answer will be used for calculation.

7. PLANNED ANALYSIS

For End-Of-Text (EoT) tables, the set of summary statistics is: N / Mean / SD / Min / Median / Max. In descriptive statistics tables, mean and median will be rounded to one additional digit than the raw individual value. SD will be rounded to one additional digit than the mean.

For tables that are provided for endpoints with some extreme data, median, quartiles and percentiles should be preferred to mean, standard deviation, minimum and maximum.

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).

The precision for percentages should be one decimal point, unless the denominator is smaller than 100 (in all treatment columns), in which case percentages are given in integer numbers. 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.

7.2.1 Baseline conditions

A summary of baseline conditions will be provided by treatment group, System Organ Class (SOC) and Preferred Term (PT). SOC will be sorted according to the standard sort order specified by EMA and PT by descending frequency over both treatment arms.

7.2.2 Concomitant therapies

Concomitant therapies will be described over several study periods, listed below.

- Previous therapies will be defined as treatments with an end date before baseline.
- Baseline therapies will be defined as treatments with a start date before baseline and a stop date after or on baseline.
- On-treatment therapies will be defined as treatments with a start date during the nintedanib treatment period defined in Section 6.1.
- Post-study drug discontinuation concomitant therapies are defined as treatments with a start date during the residual effect, post-treatment or post-study period defined in Section 6.1.

A summary of all on-treatment concomitant therapies (including baseline CTs) will be provided by treatment group, ATC3 codes and Preferred Name (PN) (sorted by alphabetical ATC class and decreasing frequency of preferred names in Nintedanib treatment arm within ATC class).

Relevant groups of therapies have been defined as Special Search Categories (SSC) or Standardised Drug Groupings (SDG).

A summary of baseline concomitant therapies, on-treatment concomitant therapies will also be performed by Special Search Category (SSC) or Standardised Drug Groupings (SDG) and Preferred Name (PN) (sorted by alphabetical SSC or SDG and decreasing frequency of preferred names within SSC or SDG).

Finally, specific tables for selected concomitant treatments that were restricted during the study will be provided (by PN):

- All on-treatment concomitant therapies (including baseline CTs)
- All concomitant therapies (including baseline CTs, on-treatment CTs)

~~Non-drug therapies will be included as coded items using the current Medical Dictionary for Regulatory Activities (MedDRA) version in use at BI at the time of database lock. They will be summarised by MedDRA system organ class (SOC) and Preferred Term. The CTR table will show the counts of patients with a condition in each SOC present (SOC sorted by standard European Medicines Agency (EMA) order) and then the conditions (preferred terms) under that SOC in descending order of overall prevalence.~~

7.3 TREATMENT COMPLIANCE

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

7.4 PRIMARY ENDPOINT

7.4.1 Primary analysis of the primary endpoint

The primary analysis will be conducted on the RS set. Only descriptive statistics are planned for this section of the report.~~The analysis of the primary endpoint will be conducted in accordance with Section 7.3.1 of the CTP.~~

7.4.2 Sensitivity analysis of the primary endpoint

~~Multiple imputation will be used to handle missing data as a sensitivity analysis using the RS set. All variables included in the analysis model will be included in the imputation model. In addition, after exploring the missing data mechanism and observed measurements on the blinded data additional variables may be included in the imputation model.~~

~~When there is no missing baseline information in the imputation model, regression method will be used. When there is missing baseline information in the imputation model, MCMC method will be used. For each imputed complete dataset, the primary analysis model will be~~

~~used for the analysis. The results will be pooled following the standard multiple imputation procedure.~~

7.5 SECONDARY ENDPOINTS

7.5.1 Key secondary endpoint

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

7.5.2 (Other) Secondary endpoints

The 12-week and 24-week secondary endpoints will be analyzed on the RS set. Only descriptive statistics are planned for this section of the report.~~The analyses of these secondary endpoints will be conducted in accordance with Section 7.3.2 of the CTP.~~

~~The 24-week secondary endpoints will be analyzed on the RS set. The analysis of these secondary endpoints will be conducted in accordance with Section 7.3.2 of the CTP. In the event of non-convergence, the following methods will be attempted (in order) to overcome it:~~

1. ~~Add the 'singular=1e-10' option in the model statement – This raises the threshold at which columns are declared linearly dependent (from typically 1e-12).~~
2. ~~Set 'maxiter=100' in the Proc Mixed statement – This increases the number of convergence iterations used from a default of 50.~~
3. ~~Set 'scoring=4' to specify use of the Fisher scoring algorithm in the first 4 iterations.~~
4. ~~Include the statement 'performance nothread' – this removes multi-threading from the calculations.~~

Secondary endpoints with FVC % predicted will be derived using the following formula:

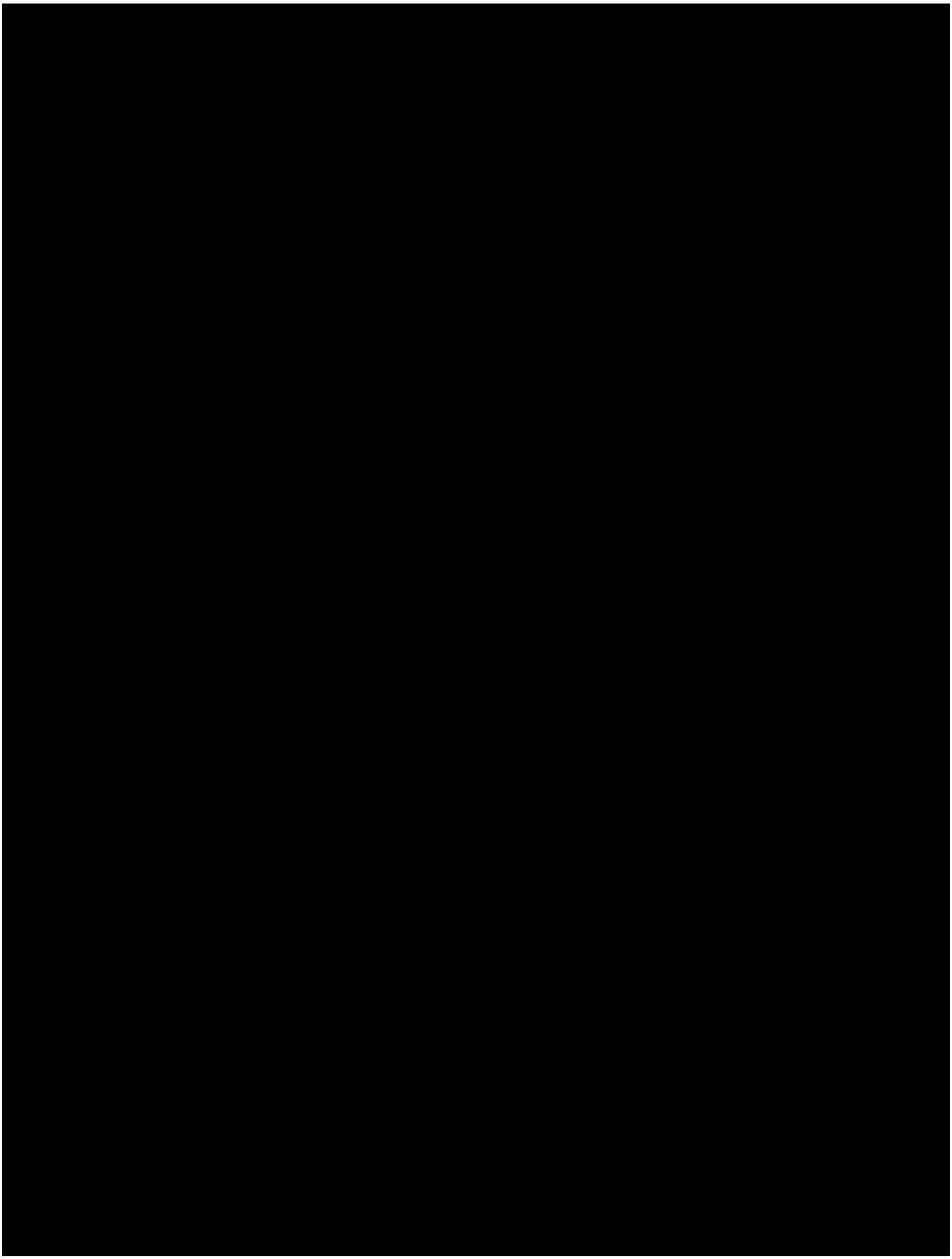
$$\text{FVC \% Predicted} = 100 \times \frac{\text{FVC [L]}}{\text{FVC Predicted [L]}},$$

Where,

$$\text{FVC Predicted [L]} = \begin{cases} 5.76 \times \text{Height(m)} - 0.026 \times \text{Age} - 4.34 \text{ if Male} \\ 4.43 \times \text{Height(m)} - 0.026 \times \text{Age} - 2.89 \text{ if Female} \end{cases}$$

Age will be as collected at Visit 1.

[redacted]



[redacted]

[redacted]

7.7 EXTENT OF EXPOSURE

The data will be analysed on the RS. A summary table showing the duration on pulmonary rehabilitation (both mean and frequency, see Section 5.4.3).

A table displaying the disposition of patients and the conclusion of patients' participation, and a table displaying the primary reason for non-inclusion/randomization will be provided.

7.8 SAFETY ANALYSIS

All safety analyses will be performed on the RS. The analysis will be performed as defined in the CTP. That is, analysis of adverse events will be restricted to nintedanib-related serious adverse events, nintedanib-non-related serious adverse events and events of special interest. Adverse events of special interest include DILI and GI Perforation.

7.8.1 Adverse Events

The analyses of AEs will be descriptive in nature and will be based on BI standards (11). No hypothesis testing is planned. All analyses of AEs will be based on the number of subjects with AEs and NOT on the number of AEs.

For analysis, multiple AE occurrence data on the CRF will be collapsed into an AE event provided that all of the following applies:

- All AE attributes are identical (LLT, intensity, action taken, therapy required, seriousness, reason for seriousness, relationship [investigator defined drug-relatedness], outcome, AE of special interest)
- The occurrences were time-overlapping or time-adjacent (time-adjacency of 2 occurrences is given if the second occurrence started on the same day or on the day after the end of the first occurrence)

For further details on summarization of AE data, please refer to the guideline "Analysis and Presentation of Adverse Event Data from Clinical Trials" (11).

The analysis of adverse events will be based on the concept of treatment emergent adverse events. That means that all adverse events occurring between first nintedanib intake on/after randomization till 28 days after last nintedanib intake will be assigned to the treatment period. All adverse events occurring before first nintedanib intake will be assigned to 'screening' or 'post-randomisation' and all adverse events occurring after last nintedanib intake will be assigned to 'residual effect', 'post-treatment' or 'post-study' (for listings only). Also, all adverse events occurring between the start of an interruption and the end of interruption will be assigned to 'off-treatment' period in the listings. For details on the treatment definition, see Section 6.1.

According to ICH E3 (10), AEs classified as 'other significant' needs to be reported and will include those non-serious and non-significant AEs with (i) 'action taken = discontinuation' or 'action taken = reduced', or (ii) marked haematological and other lab abnormalities or lead to

significant concomitant therapy as identified by the Clinical Monitor/Investigator at a MQRM.

An overall summary of adverse events will be presented. The frequency of subjects with AEs will be summarised by treatment, primary system organ class and PT (mention MedDRA levels to be displayed in the tables). Separate tables will be provided for subjects with other significant adverse events according to ICH E3 (10), for subjects with significant non-serious adverse events (only if these are defined for the project) and for subjects with serious adverse events (SAEs).

The system organ classes will be sorted by default alphabetically, PTs will be sorted by frequency (within SOC). Customized sorting orders may also be used based on trial needs, e.g. SOC sorted by frequency.

7.8.2 Laboratory data

Not applicable.

7.8.3 Vital signs

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

7.8.4 ECG

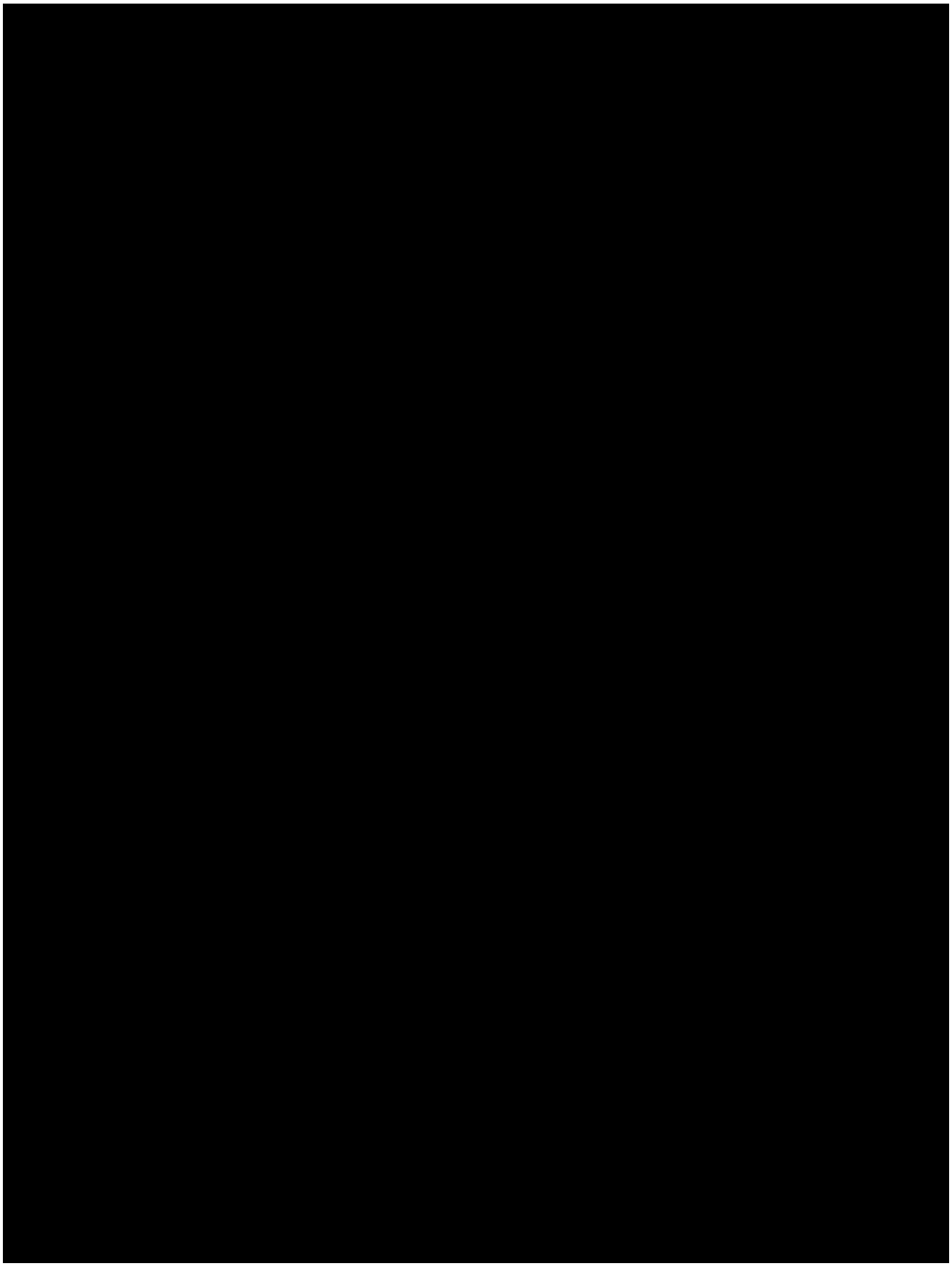
Not applicable.

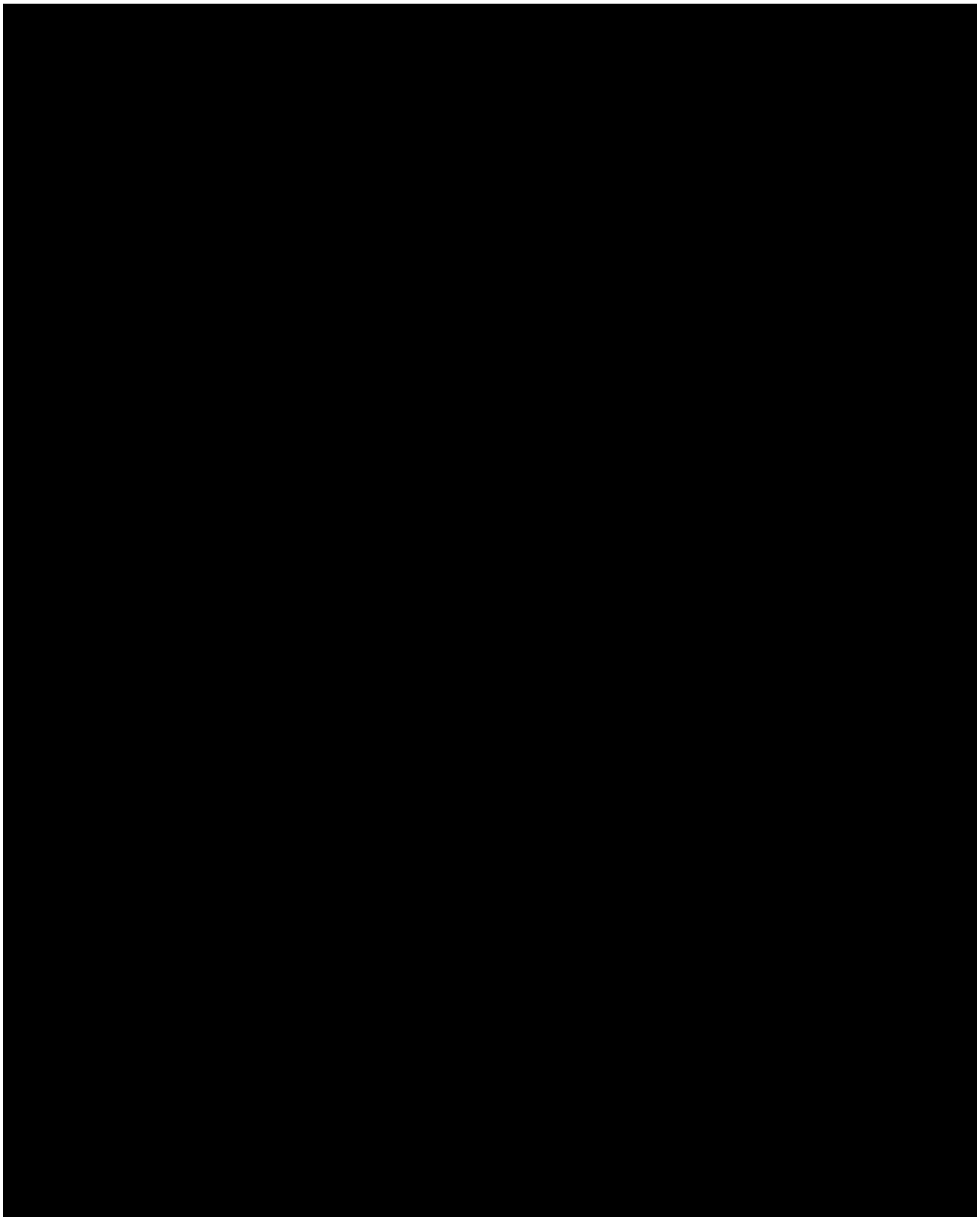
7.8.5 Others

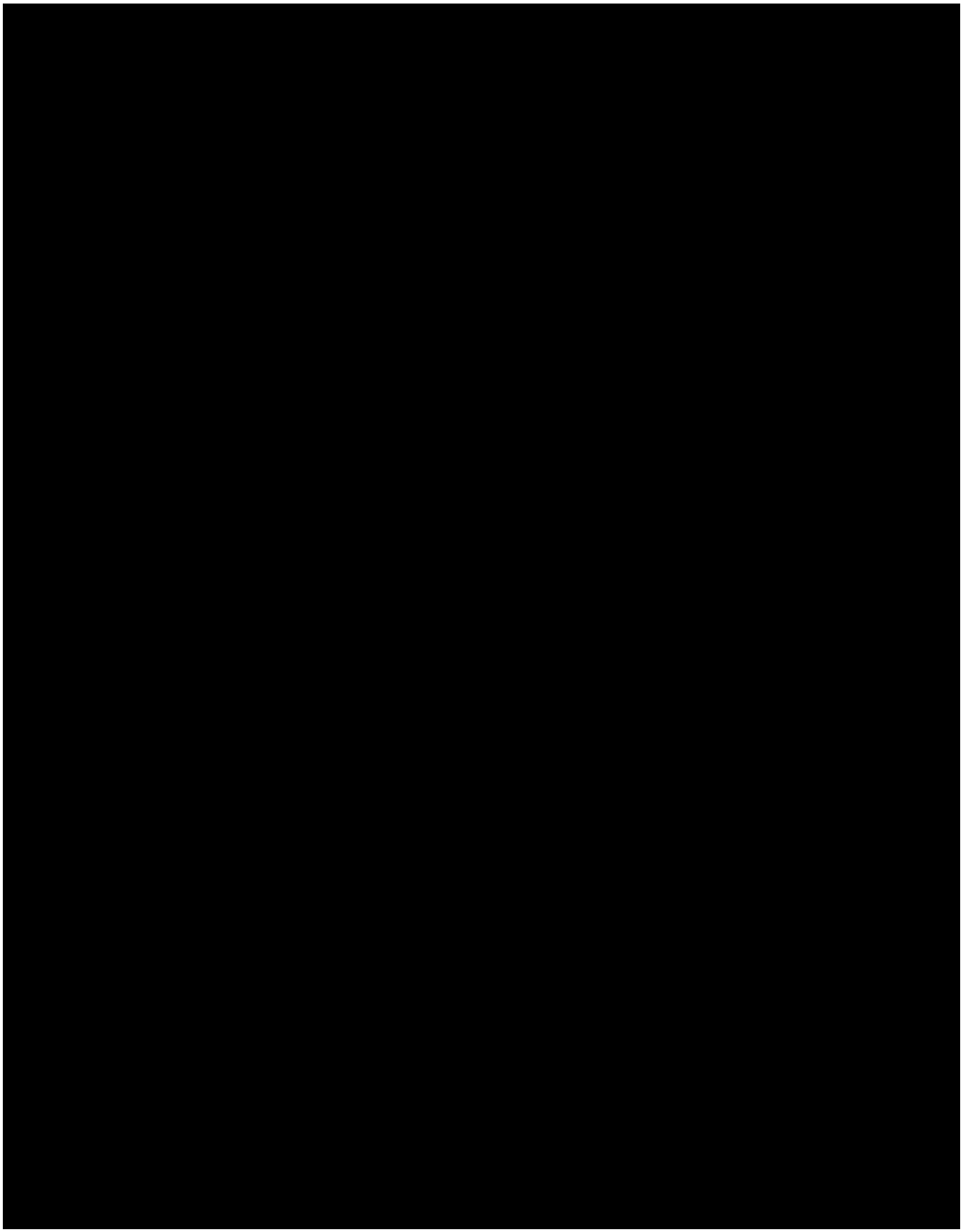
Not applicable.

8. REFERENCES

1.	*BI-KMED-BDS-HTG-0035:* "Handling of Missing and Incomplete AE Dates ", current version, Group "Biostatistics & Data Sciences", IDEA for CON.
2.	*CPMP/ICH/363/96:* "Statistical Principles for Clinical Trials", ICH Guideline Topic E9, Note For Guidance on Statistical Principles for Clinical Trials, current version.
3.	*001-MCS-50-415_RD-03:* "Clinical Trial Analysis Decision Log (template) Decision Log", current version, Group "Biostatistics & Data Sciences", IDEA for CON.
4.	*001-MCS-36-472:* "Standards and processes for analyses performed within Clinical Pharmacokinetics/Pharmacodynamics", current version, Group "Biostatistics & Data Sciences", IDEA for CON.
5.	*001-MCS-40-106_RD-03:* "Clinical Trial Protocol general template for Phase I-IV", current version, Group "Clinical Operations", IDEA for CON.
6.	*001-MCS-80-606*: "Management of Non-Compliances", current version, Group "Quality Medicine", IDEA for CON.
7.	*001-MCS-40-413:* Identify and Manage Important Protocol Deviations (iPD)", current version, Group "Clinical Operations", IDEA for CON.
8.	*001-MCS-40-135_RD-01:* "Integrated Quality and Risk Management Plan", current version, Group "Clinical Operations", IDEA for CON.
9.	REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, European Commission webpage.
10.	*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.
11.	*BI-KMED-BDS-HTG-0041:* "Analysis and Presentation of Adverse Event Data from Clinical Trials", current version, Group "Biostatistics & Data Sciences", IDEA for CON
12.	Patel AS, Siegert RJ, Brignall K, Gordon P, Steer S, Desai SR, Maher TM, Renzoni EA, Wells AU, Higginson IJ, Birring SS. The development and validation of the King's Brief Interstitial Lung Disease (K-BILD) health status questionnaire. Thorax 2012; 67 (9), 804-810 [R12-4171]







10. HISTORY TABLE

Table 10: 1 History table

Version	Date (DD-MMM-YY)	Author	Sections changed	Brief description of change
Final	**18-SEP-2020**	[redacted]	None	This is the final TSAP