


**TRIAL STATISTICAL ANALYSIS PLAN**
**c36448622-01**

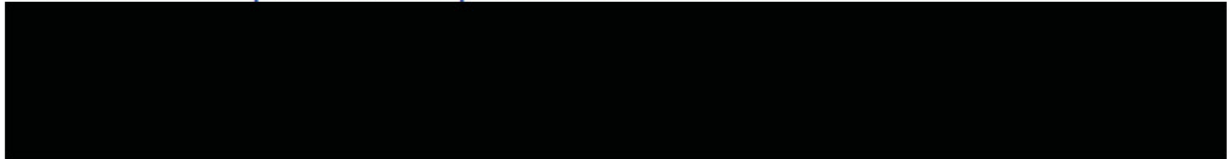


<b>BI Trial No.:</b>	1346-0038
<b>Title:</b>	<p>A phase II randomized, double-blinded, placebo-controlled parallel group trial to examine the efficacy and safety of BI 425809 once daily with adjunctive Computerized Cognitive Training over 12 week treatment period in patients with schizophrenia</p> <p>Clinical Trial Protocol (c20831949-05), including Global Protocol Amendment 1.0 (21 Dec 2018), Global Protocol Amendment 2.0 (02 Oct 2019), Global Protocol Amendment 3.0 (21 Jul 2020)</p>
<b>Investigational Product(s):</b>	BI 425809
<b>Responsible trial statistician(s):</b>	<div style="background-color: black; width: 100%; height: 80px; margin-bottom: 5px;"></div> <p>Phone: <span style="background-color: black; display: inline-block; width: 100px; height: 15px;"></span></p> <p>Fax: <span style="background-color: black; display: inline-block; width: 100px; height: 15px;"></span></p>
<b>Date of statistical analysis plan:</b>	10 OCT 2022 SIGNED
<b>Version:</b>	Final
<b>Page 1 of 36</b>	
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## 2. LIST OF ABBREVIATIONS

Term	Definition / description
AE	Adverse Event
AESI	Adverse Event of Special Interest
ALT	Alanine Aminotransferase
ANCOVA	Analysis of Covariance
AST	Aspartate Transaminase
ATC	Anatomical Therapeutic Chemical
AUC	Area under the curve
AUC <sub>0-tz</sub>	Area under the concentration-time curve of the analyte in plasma over the time interval from 0 to the last quantifiable data point
████	████████████████████
CCT	Computerized Cognitive Training
████	██
CI	Confidence Interval
C <sub>max</sub>	Maximum measured concentration of the analyte in plasma
COVID-19	Coronavirus Disease 2019
C-SSRS	Columbia Suicidal Severity Rating Scale
DILI	Drug Induced Liver Injury
GlyT1	Glycine Transporter 1
gMean	Geometric Mean
IPD	Important Protocol Deviation
MATRICS	Measurement and Treatment Research to Improve Cognition in Schizophrenia
MCCB	MATRICS Consensus Cognitive Battery
MedDRA	Medical Dictionary for Drug Regulatory Activities
M.I.N.I.	Mini-International Neuropsychiatric Interview
MMRM	Mixed-effect Model Repeated Measures
PANSS	Positive and Negative Syndrome Scale
PoC	Proof-of-concept
████	██
PT	Preferred Term
REML	Restricted Maximum Likelihood

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Term	Definition / description
REP	Residual Effect Period
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SCoRS	Schizophrenia Cognition Rating Scale
SOC	System Organ Class
	
WHO DD	World Health Organization Drug Dictionary

### **3. INTRODUCTION**

As per International Conference on Harmonisation (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 Trial Statistical Analysis Plan (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 [REDACTED] if not specified otherwise. [REDACTED]





## 5. ENDPOINTS(S)

The primary objective of this trial is to provide proof-of-concept (PoC) data to assess the effect on cognition of oral once daily administration of BI 425809 given for 12 weeks in patients with schizophrenia on stable antipsychotic treatment and adjunctive computerized cognitive training (CCT).

Other objectives of this trial are to explore endpoints to assess functioning and well-being of patients with schizophrenia, and to evaluate safety and pharmacokinetics of BI 425809.

Endpoints in this trial and their associated measurement time points are listed in Table 5: 1.

Table 5: 1 Endpoints and time points of measurement

Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6 (e)EoT	Follow-up
Screening	Baseline	Week 3	Week 6	Week 9	Week 12 (EOT) / eEOT	Week 16 / eEoT + 28 day
Day -28 to -1	Day 1	Day 22	Day 43	Day 63	Day 84	(e)EoT + 28
MCCB	MCCB		MCCB		MCCB	
PANSS	PANSS		PANSS		PANSS	
SCoRS*	SCoRS				SCoRS	
	████				████	
	██████				██████	
	██				██	
	██████				██████	
C-SSRS	C-SSRS	C-SSRS	C-SSRS	C-SSRS	C-SSRS	C-SSRS
CCT**	CCT**					
		██	████	████	████	

\*Screening SCoRS is added in Global Protocol Amendment 3 (version 4.0).

\*\*CCT usage and performance is recorded and assessed throughout the run-in/screening period and the on-treatment period.

### 5.1 PRIMARY ENDPOINT(S)

The primary endpoint is

- Change from baseline in MCCB neurocognitive composite T-score after 12 weeks of treatment

The primary endpoint will be used as defined in CTP Section 5.1.

#### MCCB

MCCB neurocognitive composite T-score is derived from the 6 domains: 1) Speed of Processing, 2) Verbal Learning, 3) Working Memory, 4) Reasoning and Problem Solving, 5) Visual Learning, and 6) Attention/Vigilance. A higher score indicates better cognitive function.

## **5.2 SECONDARY ENDPOINT(S)**

### **5.2.1 Key secondary endpoint(s)**

Not applicable. No key secondary endpoints in this trial.

### **5.2.2 Secondary endpoint(s)**

The secondary efficacy endpoints are:

- Change from baseline in MCCB overall composite T-score after 12 weeks of treatment
- Change from baseline in SCoRS total score after 12 weeks of treatment
- Change from baseline in PANSS total score after 12 weeks of treatment

The secondary safety endpoints is:

- Percentage of patients with (S)AEs

Unless otherwise specified, the secondary endpoints will be used as defined in CTP Section 5.

#### MCCB

MCCB overall composite T-score is derived from all 7 domains: 1) Speed of Processing, 2) Verbal Learning, 3) Working Memory, 4) Reasoning and Problem Solving, 5) Visual Learning, 6) Attention/Vigilance, and 7) Social Cognition.

#### SCoRS

SCoRS interviewer total score will be used for secondary endpoint analysis.

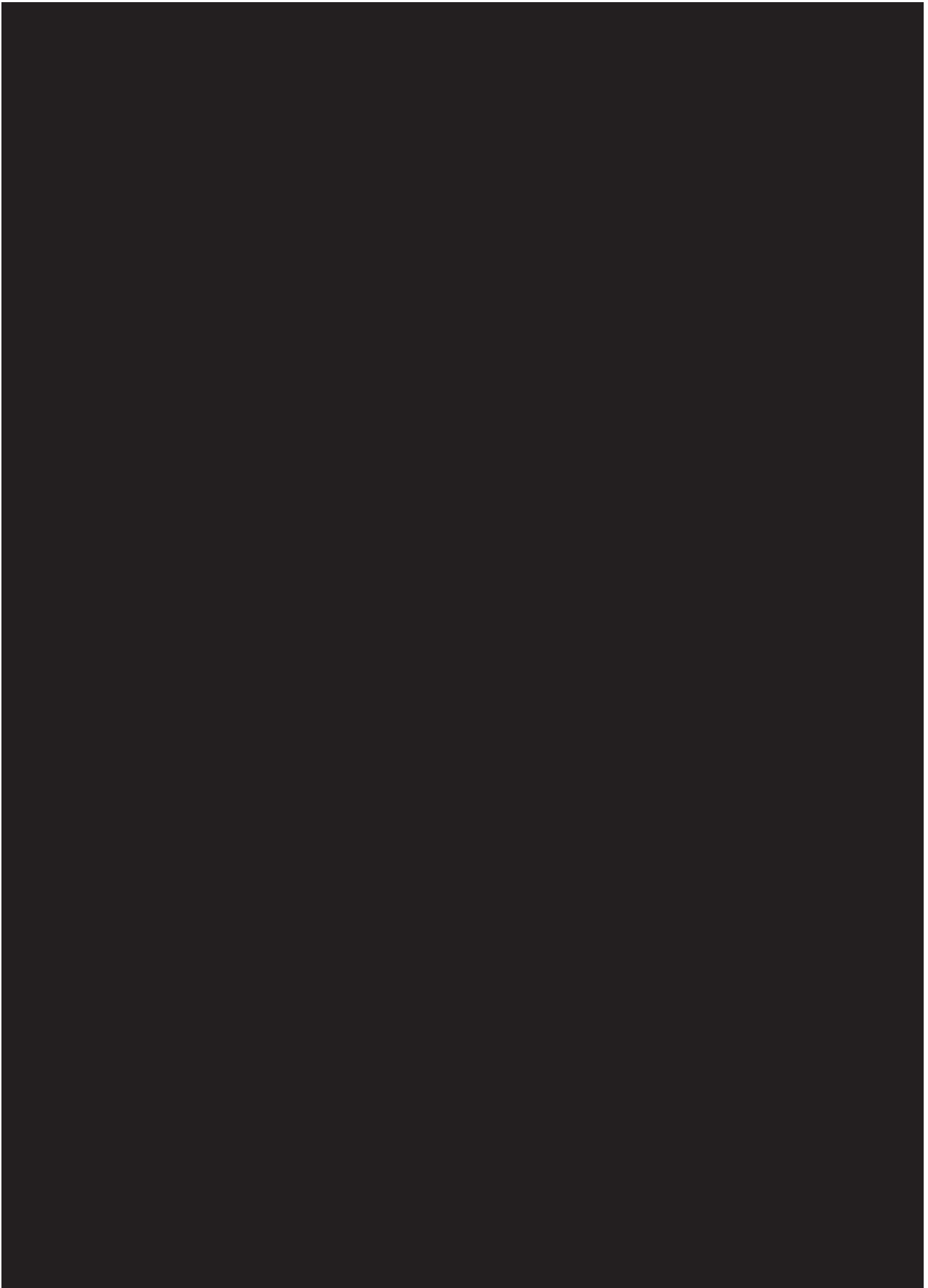
#### PANSS

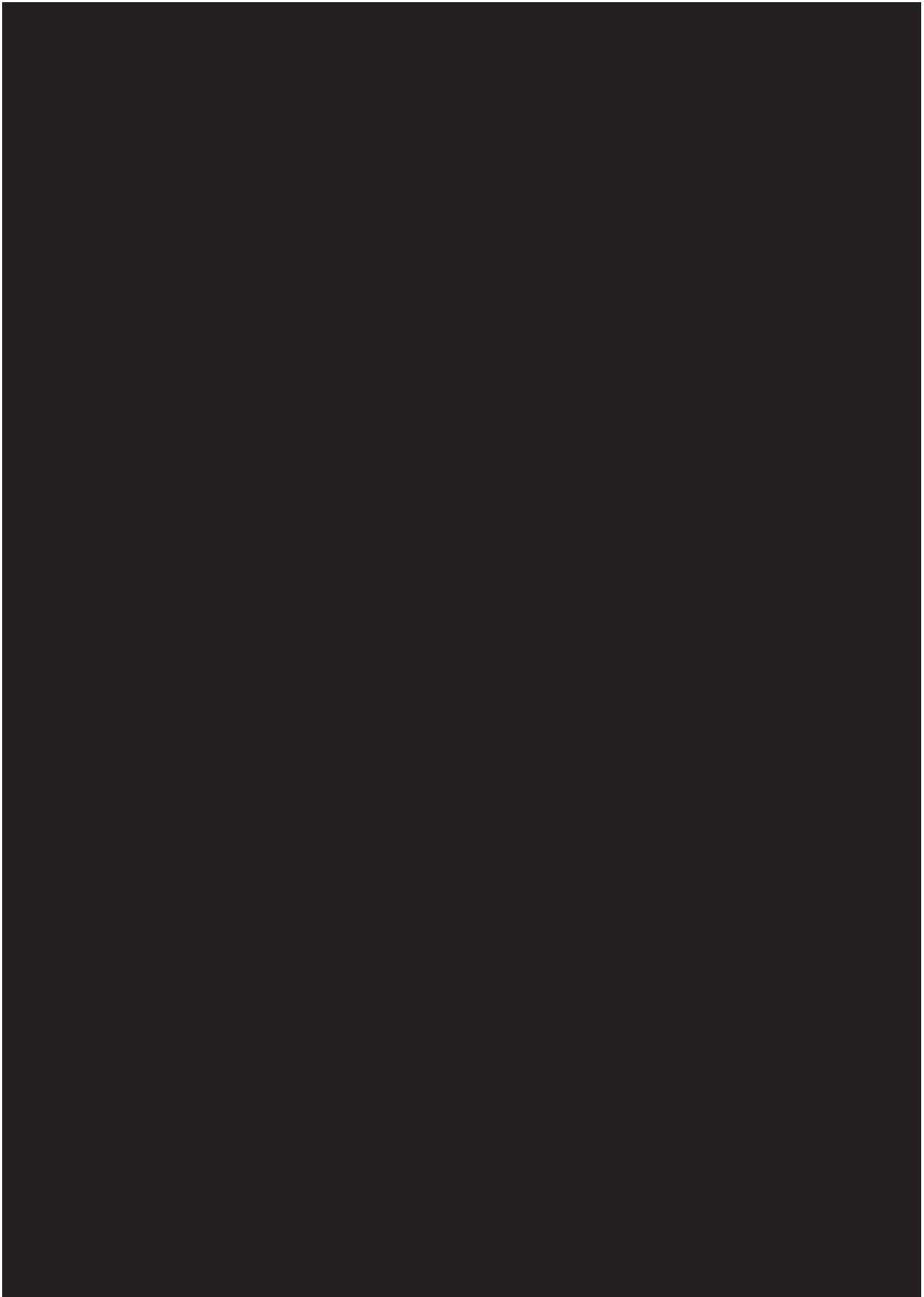
PANSS has 30 items, each rated from 1 to 7 points. The PANSS total score will be calculated as the summation of the item scores, leading to a total score ranging from 30 to 210.

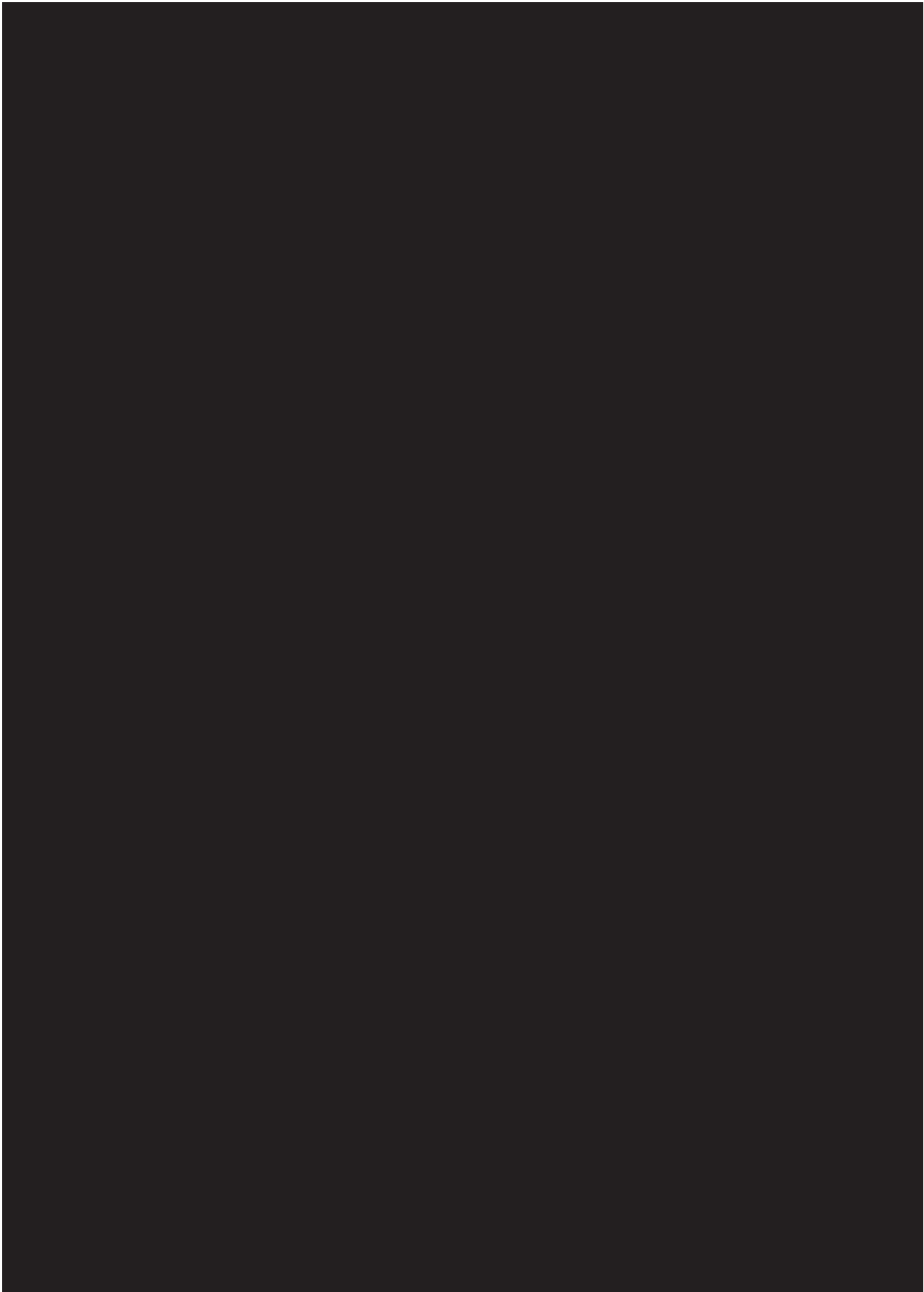
The PANSS total score is calculated only if the number of missing item scores is  $\leq 6$  (i.e.  $\leq 20\%$  of the 30 items). Otherwise, the total score will be left as missing. See [Section 6.6](#) for imputation and derivation rules.













## 6. GENERAL ANALYSIS DEFINITIONS

### 6.1 TREATMENT(S)

For basic study information on treatments to be administered, assignment of treatment groups, selection of doses, refer to CTP Section 4.

Table 6.1: 1 lists the two treatment arms in this study. Table 6.1: 2 defines the analysing treatment period for safety analysis. For this study, the residual effect period (REP) is defined as 11 days after the last dose of trial medication.

Table 6.1: 1 Treatment descriptions

Long Name	Short Name
Placebo + Computerized Cognitive Training	Placebo + CCT
BI 425809 10 mg + Computerized Cognitive Training	BI 10 mg + CCT

Table 6.1: 2 Analysing treatment periods (same for all treatment groups)

Analysing Treatment Period	Start Date	End Date (inclusive)
Screening	Date of informed consent	Date of the first treatment administration – 1 day
On-Treatment	Date of the first treatment administration	Date of the last treatment administration + REP
Follow-up	Date of the last treatment administration + REP + 1 day	Date of the last per protocol visit

Residual effect period (REP) is defined as 11 days after the last dose of study medication.

### 6.2 IMPORTANT PROTOCOL DEVIATIONS

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

Identification of iPD will be finalized at database lock (DBL). For iPDs identifiable only from unblinded data, rules are pre-specified in the DV domain specification.

### 6.3 SUBJECT SETS ANALYSED

The following patient analysis sets are defined:

- **Randomized Set (RS):** includes all patients who signed informed consent and were randomized to receive either BI 425809 + CCT or placebo + CCT. Patients will be analysed as randomized.



- **Treated Set (TS):** includes all patients in RS who were treated with at least one dose of the trial regimen (including both drug and CCT). TS will be used for safety analyses as well as demographics and baseline characteristics and treatment regimen exposure. Patients will be analysed under the actual trial regimen received at randomization.
- **Full Analysis Set (FAS):** includes all patients in TS who had non-missing baseline and at least one non-missing post-baseline on-treatment measurement of the primary efficacy endpoint. FAS will be used for efficacy analyses. Patients will be analysed as randomized.



Table 6.3: 1 Subject sets analysed

Class of endpoints	Subjects Sets Analysed				
	TS	FAS			
Primary endpoint		Primary analysis			
Secondary efficacy endpoints		Primary analysis			
Safety variables	X				
Demographic/baseline variables/exposure	X				

[Redacted text]

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## 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

Unless otherwise specified, missing data will not be imputed and will remain missing. Potential outliers will be reported and analysed as observed.

### MCCB

Handling of missing data in MCCB tests will follow the MCCB Manual (available in the ISF). See [Section 10.1](#) for detailed descriptions and imputation rules.

EoT measurement of MCCB endpoints which were collected >12 days after the last study medication intake date will not be included in the analysis.

### SCoRS

For the 20-item SCoRS assessment, if six or more of the 20 items have missing response, which includes the response of “N/A”, for a subject at a visit, then the SCoRS total score for that subject at that visit is missing. If five or less of the 20 items have missing response, which includes the response of “N/A”, for a subject at a visit, then the item with missing response will be imputed first with the average of the non-missing item values for the subject at the visit, and then SCoRS total score for the subject at the visit will be derived as the sum of the non-missing item values and the imputed item values.

PANSS

PANSS total and subscale scores will be calculated as sums of their constituting item scores. If  $\leq 20\%$  of the items are missing in the calculation of the total or subscale scores, the missing items will be temporarily imputed with the mean of the non-missing item scores. The total or subscale score will then be calculated as the sum of the non-missing and imputed item scores.

For calculation of PANSS total score and the subscale scores, the maximum numbers of missing items allowed are:

PANSS total score:	6 out of 30
Positive Symptom:	1 out of 7
Negative Symptom:	1 out of 7
General Psychopathology:	3 out of 16
Emotional Expression:	0 out of 4
Emotional Experience:	0 out of 3
Marder Negative Factor:	1 out of 7

If more than the maximum allowed number of items are missing, the score will not be calculated.



## 6.7 BASELINE, TIME WINDOWS AND CALCULATED VISITS

In general, baseline value will be the measurement taken on the day of randomization (Visit 2), and prior to the first study medication administration. If this value is not available, the measurement at the screening visit (Visit 1) will be used, except for MCCB assessments.

Baseline for MCCB neurocognitive composite score and related endpoints is defined as the measurements taken at randomization (Visit 2), and prior to the first administration of the study medication.

Analysis visit will be used for by-visit summaries and analysis of efficacy endpoints. Study day windows for mapping to analysis visits are presented in Table 6.7: 1. Actual study day will be calculated starting with day of randomization as Day 1. If more than one assessment is mapped to the same post-baseline analysis visit, the closest assessment to the planned study day will be used. In case of a tie, the earlier assessment will be used.

Table 6.7: 1 Analysis visit windows

Analysis visit	Nominal Timepoint	Planned study day	Actual study day window	
			MCCB*, PANSS	Other efficacy assessments
2	Baseline	1	≤1	≤1
4	Week 6	43	2 – 60	
6/EoT	Week 12	85	≥61	≥2

\*MCCB assessments taken >12 days after the last study medication intake will not be included in the analysis.

Safety endpoints will be summarized based on nominal visits as reported in the CRFs. No re-labelling to analysis visits will be performed.

In subject data listings, all data at scheduled or unscheduled timepoints will be presented.

## **7. PLANNED ANALYSIS**

For End-Of-Text (EoT) tables of parameters [REDACTED], the set of summary statistics is: N / Mean / Standard Deviation SD / Min / Median / Max.

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.

In general, means, medians, and quantiles are presented to one more decimal place than the raw data, whereas SDs are presented to two more decimal places than the raw data. Minima and maxima are presented to the same number of decimal places as the raw data.

Tabulations of frequencies for categorical data will include all possible categories (including categories with zero count) 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. The category missing will be displayed only if there are actual missing values.

If applicable, conversion from days to weeks, months and years follows the rules below:

- $\text{weeks} = \text{days} \div 7$
- $\text{months} = 12 \times \text{days} \div 365.25$
- $\text{years} = \text{days} \div 365.25$

### **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 will be coded based on the most current version of MedDRA. A summary of concomitant diseases will be provided by treatment group, system organ class (SOC), and preferred term (PT).

Concomitant medication will be coded according to WHO DD and classified by the Anatomical, Therapeutic, Chemical (ATC) classification system. Concomitant medication will be summarized separately for psychoactive medications.

### **7.3 TREATMENT COMPLIANCE**

Only descriptive statistics are planned for this section of the report. See [Section 5.4](#) for definitions of treatment compliance and CCT compliance/exposure.

## 7.4 PRIMARY ENDPOINT(S)

### 7.4.1 Primary analysis of the primary endpoint(s)

The primary analysis is a restricted maximum likelihood (REML) based approach using the following mixed model with repeated measurements (MMRM) comparing the change from baseline in MCCB neurocognitive composite T-score after 12 weeks of treatment:

$$y_{ijkm} = \tau_{jk} + \beta_j X_i + \phi_m + \gamma Z_i + e_{ij}$$

$$e_{ij} \sim N(\mathbf{0}, \Sigma)$$

where

- $y_{ijkm}$  = response variable for subject  $i$  in age stratum  $m$  at visit  $j$  receiving treatment  $k$ ,
- $\beta_j$  = coefficient of baseline effect at visit  $j$ ,
- $X_i$  = baseline MCCB neurocognitive composite T-score of subject  $i$ ,
- $\tau_{jk}$  = effect of treatment  $k$  at visit  $j$ ,
- $\phi_m$  = effect of age stratum  $m$
- $\gamma$  = coefficient of change from screening to baseline effect,
- $Z_i$  = change from screening to baseline in MCCB neurocognitive composite T-score
- $e_{ij}$  = random error associated with visit  $j$  of subject  $i$ , independently distributed across subjects,
- $\Sigma$  = unstructured variance-covariance matrix.

The model will include fixed, categorical effects of treatment at each visit, fixed continuous effect of baseline at each visit, fixed effects of age strata ( $\leq 40$  vs.  $> 40$ ), and fixed continuous effect of change in MCCB neurocognitive composite score from screening to baseline. Visit will be treated as the repeated measure with an unstructured variance-covariance matrix used to model the within-patient measurements.

Denominator degrees of freedom will be calculated using Kenward-Roger approximation. The primary treatment comparison will be the contrast between the two treatments at the endpoint visit, i.e. Week 12.

The primary analysis will be performed on FAS. Patients will be analysed according to the actual age stratum they belong to, regardless of any treatment mis-assignment due to wrong stratum identification because such an error would have occurred before randomization and is therefore consistent with regulatory guidance.

In the event of non-convergence, the following methods will be attempted in order:

1. Add the 'singular=1e-10' option in the model statement, to raise the threshold at which columns are declared linearly dependent from the default value of 1e-12.
2. Set 'maxiter=100' in PROC MIXED statement, to increase the number of convergence iterations from a default of 50.
3. Set 'scoring=4' to specify the use of Fisher scoring algorithm in the first 4 iterations.

4. Include the statement 'performance nothread' to remove multi-threading from calculations.





## 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)

#### 7.5.2.1 Primary analysis of the secondary endpoints

Primary analysis of the secondary endpoints will be conducted on FAS. Estimated least squares mean difference between the two treatment arms will be provided together with 95% confidence intervals. Statistical model and estimation method for each secondary endpoint are described below.

#### MCCB overall composite T-score

The primary analysis of change from baseline in MCCB overall composite T-score after 12 weeks of treatment will be a REML based approach using the same MMRM as in [Section 7.4.1](#). The baseline and change-from-screening-to-baseline covariates,  $X_i$  and  $Z_i$ , will be replaced by their overall composite T-score version.

#### SCoRS interviewer total score

The primary analysis of change from baseline in SCoRS interviewer total score after 12 weeks of treatment will be an ANCOVA based approach using the following model:

$$y_{ikm} = \tau_k + \beta X_i + \phi_m + e_i$$

$$e_i \sim N(0, \sigma^2)$$

where

- $y_{ikm}$  = response variable for subject  $i$  in age stratum  $m$  receiving treatment  $k$ ,  
 $\beta$  = coefficient of baseline effect,  
 $X_i$  = baseline value of subject  $i$ ,  
 $\tau_k$  = effect of treatment  $k$ ,  
 $\phi_m$  = effect of age stratum  $m$   
 $e_i$  = random error associated with subject  $i$ , independently distributed ,  
across subjects

#### PANSS total score

The primary analysis of change from baseline in PANSS total score after 12 weeks of treatment will be a REML based approach using the following simplified MMRM from that in [Section 7.4.1](#):

$$y_{ijkm} = \tau_{jk} + \beta_j X_i + \phi_m + e_{ij}$$

where  $X_i$  = baseline score of subject  $i$ , while the other covariates and parameters are same as defined in Section 7.4.1.





## **7.7 EXTENT OF EXPOSURE**

Extent of exposure will be summarized for the treated set using descriptive statistics for days on treatment as well as frequency and percentage of subjects in the following categories: <30 days, 30 – 41 days, 42 – 59 days, 60 – 89 days,  $\geq$  90 days.

Exposure to CCT will be summarized using descriptive statistics as described in [Section 5.4](#).

## **7.8 SAFETY ANALYSIS**

All safety analyses will be performed on the treated set.

### 7.8.1 Adverse Events

Unless otherwise specified, 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. The reporting and analysis of AEs will follow the BI guideline (2). AEs will be coded with the latest version of MedDRA.

The analysis of AEs will be based on the concept of treatment emergent AEs. For this study, the residual effect period (REP) is defined as 11 days after the last dose of trial medication. That means that all AEs occurring between first drug intake till 11 days after last drug intake will be assigned to the “on-treatment” period. All AEs occurring before first drug intake will be assigned to ‘screening’ and all AEs occurring after last drug intake + 11 days will be assigned to ‘follow-up’ (for listings only). For details on the treatment definition, see [Section 6.1](#).

#### Adverse events of special interest (AESIs)

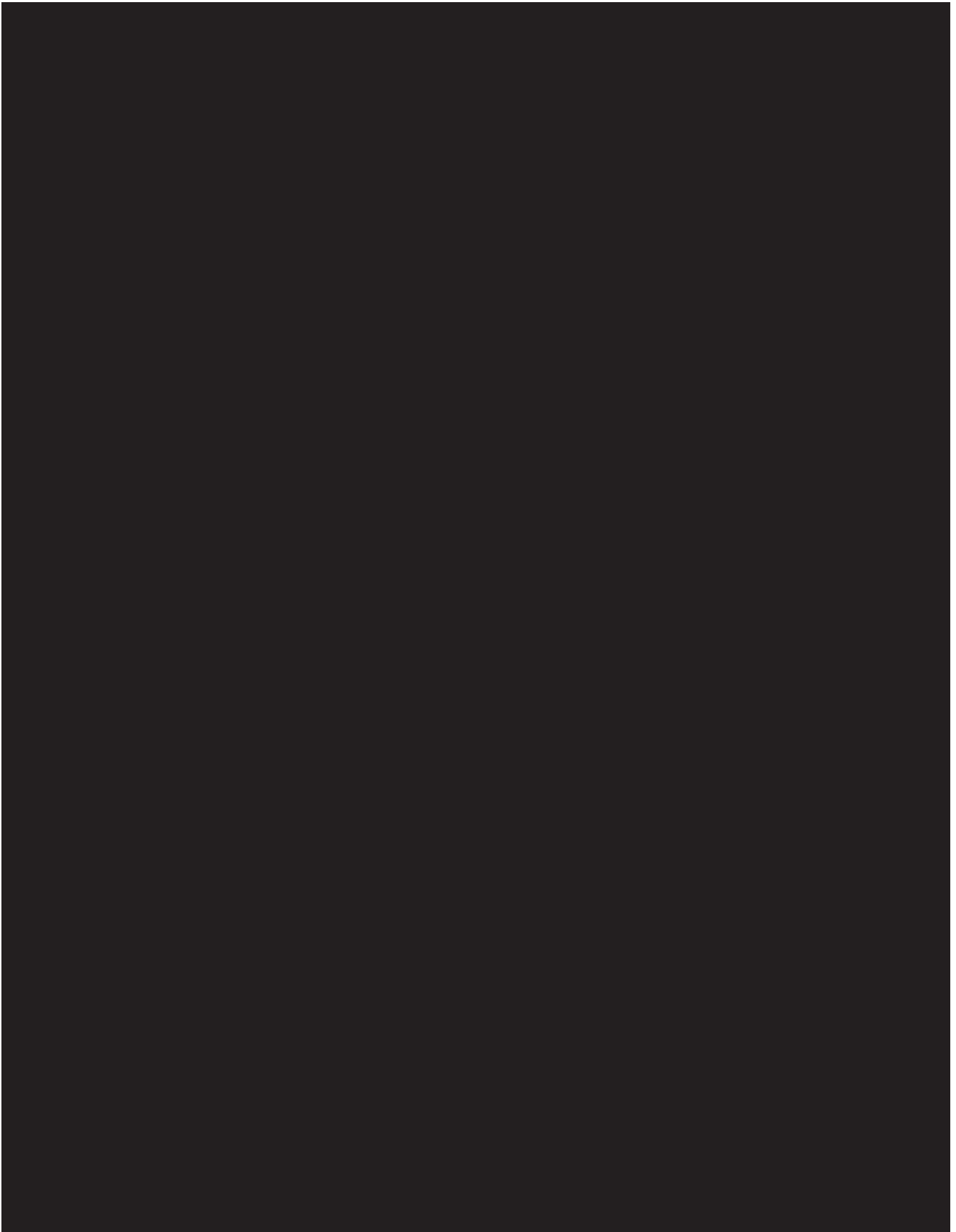
As defined in CTP Section 5.2.6.1, AESI includes hepatic injury defined by the following alterations of hepatic laboratory parameters:

- an elevation of AST (aspartate transaminase) and/or ALT (alanine aminotransferase) >3-fold ULN combined with an elevation of total bilirubin >2-fold ULN measured in the same blood draw sample, or
- aminotransferase (ALT, and/or AST) elevations  $\geq 10$ -fold ULN.

#### Other significant AE (according to ICH E3)

According to ICH E3 (6), AEs classified as "other significant" needs to be reported and will include those non-serious and non-significant AEs with

1. ‘action taken = discontinuation’ or ‘action taken = reduced’; or
2. marked haematological and other lab abnormalities or lead to significant concomitant therapy as identified by the Clinical Monitor / Investigator during medical quality review at a trial oversight meeting (TOM).



An overall summary of AEs will be presented.

The frequency of subjects with AEs will be summarised by treatment, primary system organ class and PT. Separate tables will be provided for subjects with SAEs, AEs leading to treatment discontinuation, AEs of at least moderate severity and related AEs.

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.

Separate tables will be provided for the following AEs:

- drug-related AEs
- serious AEs (SAEs)
- drug-related SAEs
- AESIs
- Other significant AE (according to ICH E3)
- AEs leading to death
- AEs leading to discontinuation of trial medication
- AEs occurred with >2% incidence in the preferred term
- AEs by intensity
- AEs occurred during the follow-up period.
- AEs related to COVID-19

## **7.8.2 Laboratory data**

The analyses of laboratory data will be descriptive in nature and will be based on BI standards [\(5\)](#).

Descriptive statistics for laboratory values will be derived and displayed visit-by-visit using converted values. Shift tables of change in laboratory parameters between baseline and worst value on treatment, between baseline and last value on treatment, and between worst and last value on treatment will also be presented.

In addition, the following will be presented for haemoglobin (Hb):

- shift tables of change in Hb between last value on treatment and last value post-treatment,
- spaghetti plots of change in Hb from baseline across time with time trend of mean and standard error,

### **7.8.3 Vital signs**

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

### **7.8.4 ECG**

Clinically relevant abnormal ECG findings will be reported and analysed as AEs.

### **7.8.5 Others**

#### Worsening Disease State as assessed by PANSS

Change in PANSS from baseline to each post-baseline visit will be presented in a data listing. Increases greater than or equal to 5 will be flagged.

#### Suicidality as assessed by the C-SSRS

C-SSRS will be summarized by counts and percentages per treatment group. The number of patients with suicidal ideation (for each type of 1 to 5 separately), suicidal behaviour (type 6 – 10), and with self-injurious behaviour without suicidal intent will be presented, overall and within subcategories. A summary will also be presented for lifetime experience. Shift table and listings will be provided.



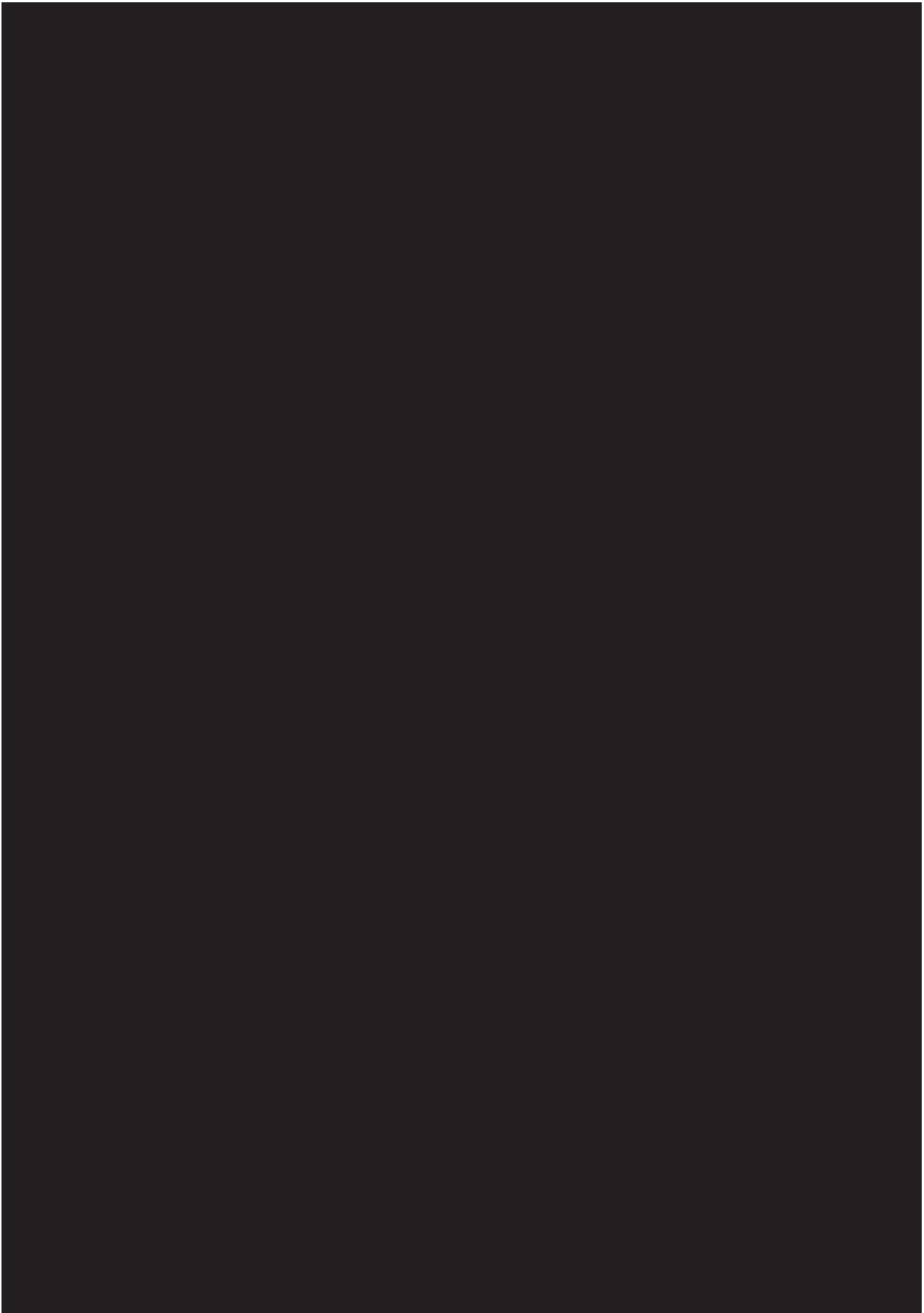
## **8. TIMEPOINT OF RELEASE OF TREATMENT INFORMATION**

The treatment information will be released to unblind the trial database after the last patient has completed their End-of-Study/Follow-up visit and all data has been entered and cleaned as defined in the “Data Ready to be Unblinded and/or Final Trial Closure Notification” (RUN) form.



## 9. REFERENCES

1.	<i>CPMP/ICH/363/96</i> : "Statistical Principles for Clinical Trials", ICH Guideline Topic E9, Note For Guidance on Statistical Principles for Clinical Trials, current version.
2.	<i>BI-KMED-BDS-HTG-0066</i> : "Analysis and Presentation of Adverse Event Data from Clinical Trials", KMed.
3.	<i>BI-KMED-BDS-HTG-0035</i> : "Handling of Missing and Incomplete AE Dates", KMed.
4.	<i>BI-KMED-TMCP-MAN-0012</i> : "Standards and processes for analyses performed within Clinical Pharmacokinetics/Pharmacodynamics", KMed.
5.	<i>BI-KMED-BDS-HTG-0042</i> : "Handling, Display and Analysis of Laboratory Data", KMed.
6.	<i>CPMP/ICH/137/95</i> : "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.
7.	Little, R. J. & Rubin, D. B. (2002). <i>Statistical Analysis with Missing Data</i> (2 <sup>nd</sup> ed). New York: John Wiley & Sons.





## 11. HISTORY TABLE



Table 11: 1 History table

<b>Version</b>	<b>Date</b>	<b>Author</b>	<b>Sections changed</b>	<b>Brief description of change</b>
1	10-OCT-2022		None	This is the final TSAP

**APPROVAL / SIGNATURE PAGE**
**Document Number: c36448622**
**Technical Version Number:1.0**
**Document Name: 8-01-tsap**

**Title:** A phase II randomized, double-blinded, placebo-controlled parallel group trial to examine the efficacy and safety of BI 425809 once daily with adjunctive Computerized Cognitive Training over 12 week treatment period in patients with schizophrenia

**Signatures (obtained electronically)**

Meaning of Signature	Signed by	Date Signed
Approval-Clinical Program 		11 Oct 2022 00:38 CEST
Approval-Medical Writer		11 Oct 2022 08:39 CEST
Author-Trial Clinical Pharmacokineticist		11 Oct 2022 10:12 CEST
Approval-Project Statistician		11 Oct 2022 14:30 CEST
Author-Trial Statistician		14 Oct 2022 04:44 CEST
Approval-Clinical Trial Leader		17 Oct 2022 23:06 CEST

**(Continued) Signatures (obtained electronically)**

<b>Meaning of Signature</b>	<b>Signed by</b>	<b>Date Signed</b>
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