
**Statistical analysis plan**

This supplementary material has been provided by the authors to give readers additional information about their work.
STATISTICAL ANALYSIS PLAN

Effects of selective serotonin re-uptake inhibition on MOrbidity, mOrtality and mood in Depressed Heart Failure patients

A double-blind, randomised, placebo-controlled, parallel group study to determine the effects of serotonin re-uptake inhibition with the SSRI escitalopram on morbidity, mortality and mood in depressed patients with chronic systolic heart failure

MOOD-HF

Principal Investigator: Prof. Dr. Christiane E. Angermann
Comprehensive Heart Failure Centre
University Hospital Würzburg and University of Würzburg

Biometrician: Prof. Dr. Dr. Götz Gelbrich
Institute of Clinical Epidemiology and Biometry
University of Würzburg

Study Management: Comprehensive Heart Failure Centre and
Clinical Trial Centre Leipzig

Sponsor: University of Würzburg

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GENERAL INFORMATION

Signatures

This analysis plan was completed in its first version by 26.11.2015 and amended by 10.02.2015. The definitions in chapters 3, 4 and 5, and sections 7.1, 7.2, 7.3 and 7.4 were not altered by amendments after 26.11.2015. No changes to this analysis plan were made after 10.02.2015.

This analysis plan is hereby approved. Any deviation from the specifications made herein require an amendment in writing. Any additional analyses carried out on the trial data not specified in this analysis plan have to be labelled as “not pre-specified”.

Co-Chair of Steering Committee I: ___________________ 10. Feb. 2015 ___________________

Date Signature

Co-Chair of Steering Committee II: ___________________ 10. Feb. 2015 ___________________

Date Signature

Principal Investigator: ___________________ 10. Feb. 2015 ___________________

Date Signature

Senior Biometrician: ___________________ 10. Feb. 2015 ___________________

Date Signature
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>6MWD</td>
<td>six minute walk distance</td>
</tr>
<tr>
<td>AE</td>
<td>adverse event</td>
</tr>
<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>CRF</td>
<td>case report form</td>
</tr>
<tr>
<td>dpw</td>
<td>drinks per week</td>
</tr>
<tr>
<td>ECG</td>
<td>electrocardiography</td>
</tr>
<tr>
<td>eGFR</td>
<td>estimated glomerular filtration rate</td>
</tr>
<tr>
<td>HF</td>
<td>heart failure</td>
</tr>
<tr>
<td>ITT</td>
<td>intention to treat</td>
</tr>
<tr>
<td>LV</td>
<td>left ventricular</td>
</tr>
<tr>
<td>MADRS</td>
<td>Montgomery–Åsberg Depression Rating Scale</td>
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<tr>
<td>MDRD</td>
<td>Modification of Diet in Renal Disease</td>
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<tr>
<td>NYHA</td>
<td>New York Heart Association</td>
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<tr>
<td>OSM</td>
<td>on study medication</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>Nine-item Patient Health Questionnaire</td>
</tr>
<tr>
<td>QTc</td>
<td>corrected QT time (from ECG)</td>
</tr>
<tr>
<td>SAE</td>
<td>serious adverse event</td>
</tr>
<tr>
<td>SAP</td>
<td>statistical analysis plan</td>
</tr>
<tr>
<td>SI</td>
<td>international system of units</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
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</table>
Funding and registration information

This trial was funded by the German Federal Ministry of Education and Research (BMBF),
grant no. GFVT01024505, and co-funded by H. Lundbeck A/S, Kopenhagen, Denmark.

The study has been registered at controlled-trials.com, the unique identifier is ISRCTN 33128015.

The study carries the EudraCT-No: 2007-006609-25
1 INTRODUCTION

This document describes the Statistical Analysis Plan (SAP) for the Clinical Trial “Effects of selective serotonin re-uptake inhibition on morbidity, mortality and mood in depressed heart failure patients (MOOD-HF). It describes in detail the analyses that were specified in the study protocol. It also outlines additional analyses that do not require a protocol amendment, but should be performed in regard of issues raised during the course of this study.

The MOOD-HF trial is a double-blind, randomized, parallel group, placebo controlled, multicenter clinical trial. Chronic heart failure (HF) patients with co-morbid depression, detected by screening with the PHQ-9 questionnaire and verified by the diagnosis of a psychiatric specialist, are randomly allocated to escitalopram or placebo. The trial aims to compare all-cause mortality and unplanned hospitalisation, load of depressive symptoms, clinical and laboratory parameters of CHF severity in between the intervention and the control group, and to analyse the relationship between changes in depression and changes in CHF severity.

The design and methods of the MOOD-HF trial are described in the study protocol and were published [Angermann 2007], although major modifications of the protocol were performed after publication (see below).

There were 11 amendments to the study protocol. The most important changes were restrictions of eligibility and dosage in regard of a warning that escitalopram increases QTc, prolongation of recruitment time due to lower than expected inclusion rate, and reduction of target sample size in regard of the rate of primary endpoints being much higher than expected. The final protocol version including all amendments can be found at http://www.chfc.ukw.de/fileadmin/uk/chfc/Dokumente/Studien_Flyer/MOOD-HF_Pruefplan.pdf
2 **OBJECTIVES**

2.1 **Primary Outcome**

To investigate the effects of selective serotonin re-uptake inhibition with the SSRI escitalopram on morbidity and mortality in depressed patients with chronic HF. The primary endpoint is the time to a first clinical event, either death or unplanned hospitalisation, whichever occurs first, for any reasons.

2.2 **Secondary Outcomes**

Major secondary objectives:

- To estimate the reduction of depression attributable to escitalopram as measured by the PHQ-9 and MADRS scales.
- To check whether reduction of morbidity and mortality possibly found in the primary analysis is mediated by reduction of depression.

Further secondary objectives:

To investigate the effects of treatment with escitalopram, accounting for patient co-variables (sociodemographic, history, type and baseline severity of heart failure, other co-morbidity, history of vs. newly diagnosed depression), on the following secondary endpoints:

- Time alive out of hospital
- Cardiovascular morbidity and cardiovascular mortality
- General and disease-related quality of life as measured by the SF-36 and KCCQ scales, as well as anxiety as measured by the PHQ-GAD-7 scale
- Extent of cognitive dysfunction as assessed by the MMSE
- Clinical parameters of severity of CHF (e.g. NYHA class)
- Laboratory parameters of severity of CHF (e.g. natriuretic peptides)
- Functional parameters of severity of CHF (e.g. left ventricular ejection fraction, left ventricular end-diastolic volume, systolic tricuspid valve pressure gradient)
- Adherence to study medication (pill count, escitalopram plasma levels)
- Adherence to CHF medication
- Safety and tolerability of study medication
• Frequency and severity of adverse events

• Function of the sympathetic nervous system (e.g. mean heart rate, heart rate variability, arrhythmias, plasma cortisol, circadian variation of cortisol in saliva, urine norepinephrine excretion, plasma aldosterone)

• Parameters of systemic inflammation

Investigations triggered by DSMB decisions

• ECG time intervals

Concomitant investigations:

• Prevalence of suspect depression in the CHF population and positive predictive value of the PHQ-9 (SCREEN-MOOD)

• Platelet function and coagulation (THROMBO-MOOD, substudy)*

• Arterial stiffness and endothelial function (VASO-MOOD, substudy)*

• Genetic predisposition for depression (GENE-MOOD, substudy)*

• Osmoregulation and sodium homeostasis (OSMO-MOOD, substudy)*

• Cost-effectiveness analysis*

* These exploratory analyses will not be addressed in this SAP
3 ANALYSIS SETS AND MODES OF ANALYSIS

3.1 Intention to treat (ITT)

The ITT analysis set consists of all patients who were randomised and not excluded (see below) and ingested at least one dose of study medication. Subjects will be evaluated in the group they have been randomised for, regardless of the treatment they have actually received.

All analyses will be carried out following the ITT principle, unless specified otherwise.

3.2 On study medication (OSM)

The OSM analysis set consists of all patients who received the study medication. Patients who have stopped the study medication but continued to attend the study visits will be evaluated in the OSM set until the date when the study medication was stopped and not continued thereafter.

OSM analyses of time-to-event endpoints and of repeat measurements should also include an analysis carried out on the ITT set including an OSM indicator variable as a time-dependent covariate.

3.3 Patients withdrawn or excluded

Patients who have withdrawn from the study prior to their scheduled end-of-study date will be evaluated in the ITT or OSM set, whichever applies, until the date of withdrawal. Data of SAE outcomes beyond the date of withdrawal should be included in the reporting of SAE that occurred during participation in the study.

For patients excluded after erroneous randomisation this fact and its circumstances will be reported separately. These patients will not be included in any analyses. No data of these patients will be reported unless they are necessary to understand the procedure of inclusion into, and subsequent exclusion from the study, or unless they represent a safety issue.
4 CLASSIFICATION OF ENDPOINTS

4.1 Data for the primary outcome

All hospitalisations are adjudicated by a clinical endpoint committee (CEC). The members of the CEC are independent of all other study procedures and independent from the principal investigator. The CEC proceeds according to its charter, which has been approved by the principal investigator and the senior biometrician of the trial prior to any adjudication. The final results of the endpoint adjudication are entered into the trial database.

4.2 Safety data

Serious adverse events (SAE) are reported to the Clinical Trial Centre Leipzig. Here they are evaluated for the first time, processed into the database and cross-checked against AE reports. A secondary evaluation will be made by the clinical coordinating investigator or a deputy of him/her. It should be ensured that a SAE is never evaluated by the same person who documented the SAE.
5 HANDLING OF SUSPECT AND MISSING DATA

5.1 Suspect data

Suspect data should be queried as prescribed in the database specification. Queries should be resolved before the closure of the database. If this process does not lead to a correction of the data, they should remain in the database unless they are impossible.

Data are impossible if under no circumstances they could have been measured or observed. For example, a laboratory value that is incompatible with a human being alive is impossible. Impossible data should be removed at the database level after approval by the principal investigator and the trial biometrician. A record of removed impossible data should be kept at the Clinical Trial Centre Leipzig.

5.2 Analyses of suspect data

In general, data that have been queried as being suspect but have not been corrected will be included into analyses as all other data. If it is assumed that the result of an analysis could have been substantially altered by possibly wrong data, a sensitivity analysis should be carried out by repeating the same analysis excluding the data being considered suspect.

5.3 Reporting of missing data

The number of missing data should be reported in the descriptive statistics presenting these data for the first time. Any analysis should specify the number of cases included.

5.4 Dependent variables

Analyses of a single dependent variable will omit cases with the missing dependent variable. If considered necessary, a sensitivity analysis will be carried out with imputed values for the missing data. If more than 10% of data are missing, multiple imputation should be applied.

Analyses of repeated measurements will use general estimating equations. If more than 10% of the data are missing, one or more indicators for missing values (as appropriate) should be included as predictor variables in order to check whether missing data at one visit are associated with higher or lower values at another visit.
5.5 Group variables and co-variables

If data are presented in subgroups and values are missing the group variable, the missing cases should be presented in a separate subgroup.

If missing values of predictor variables would cause a substantial loss in the number of available cases in multiple regression analyses, a missing category should be added for the respective variable, or imputation should be used, specifying the reason for the mode of imputation. Consider multiple imputation when more than 10% of the data are missing.
6 PRESENTATION OF BASELINE CHARACTERISTICS

6.1 General procedures

Data will be presented in total and by randomised treatment. No p-values will be reported as assignment to groups was random, hence there is nothing to test whether some imbalance between groups might have occurred by chance or have an essential background.

**Categorical data:** Frequencies and percentages of categories will be reported. If there were missing values, the missing category should be included, and percentages in regard of both the entire sample and valid data should be displayed. Percentages are rounded to integers. If a percentage rounds to 0 or 100 but does not equal these numbers, “<1” or “>99” should be displayed, respectively.

**Quantitative data:** Unless specified otherwise, means and standard deviations will be reported. For substantially skewed data, means and quartiles will be used instead. For basic data (e.g., age, depression questionnaire sum score), the range and/or the frequencies of the categorised variable should be shown in addition. The number and percentage of missing values should be displayed unless there are none.

6.2 Demography

Report the sex, age and ethnicity from the sociodemography section of CRF page B-1.

Age is the difference between date of birth, assuming the 15th as the day of the month, and the date of the informed consent from CRF page R. Report also the range of ages.

6.3 Physical examination

Report the data from the physical examination section on CRF page B-1 and the following variables, which need to be computed:

- Body Mass Index
- Body Surface Area according to Mosteller’s formula
- Waist:hip ratio
6.4 Description of heart failure

Report the data from HF signs and symptoms, classification of severity (NYHA class) and main aetiology of HF and physical activity sections on CRF page B-1.

6.5 Cardiovascular history

Report the data from all sections on CRF page B-2.

Alcohol consumption should be reported only categorically: 0, >0-14, and >14 dpw.

For cause of HF, report congenital HF, primary valve disease and other pooled into one category “other”.

6.6 Concomitant diagnoses

Report the data from this section on CRF page B-3.

6.7 ECG

Report the data from the ECG section on CRF page B-3.

6.8 Six minute walk test

Report the data from this section on CRF page B-3.

For stopping criteria, report a category “none specified” if none has been specified unless specification was due.

6.9 Medication

Report the following, based on the from the medication section on CRF page B-4:

- Frequencies of each medication class
- For joint ACE inhibitor and/or AT1 receptor antagonists, and for beta-blockers, compute the % of recommended daily dose and report as quantitative variables, and report the proportion of patients receiving ≥50% of recommended daily dose and of those receiving recommended target doses and above
6.10 **Echocardiography**

Report the data from the echocardiography section on CRF page B-5.

If LV volumes are missing, impute by the Teichholz formula from M mode data.

Compute E/A and E/e’ and report as quantities. Also report the frequencies of E/A<0.5, E/A>3 and E/e’>15.

6.11 **Laboratory data**

Proceed as follows using the data from the laboratory section on CRF pages B-6/7:

Convert all values to SI units. Report as quantities.

Also report conventional units for haemoglobin and creatinine.

Compute the following and report as specified:

- Anaemia (WHO definition), categorical
- Estimated glomerular filtration rate (MDRD formula), quantity
- Renal dysfunction (eGFR<60 mL/min/1.73m²), categorical
- NTproBNP, quantity (skewed)

6.12 **Study medication**

Report the starting doses from CRF page B-7.

6.13 **Questionnaires**

Scores of the following questionnaires recorded at the inclusion visit will be presented:

- MADRS sum score (quantity) + categories (0-12, 13-21, 22-28, ≥29)
- PHQ-9 sum score (quantity) + categories (0-8, 9-11, 12-16, ≥17)
- SF-36, 8 scales according to manual (quantities)
- KCCQ Clinical summary scale and Functional Status summary scale
- GAD-7 sum score
- MMSE sum score
7 OUTCOME MEASURES AND ANALYSES

Unless specified otherwise, outcomes will be analysed by the following methods:

- Time-to-event endpoints: Cox regression + Kaplan-Meier incidence curves
- Quantitative variables: general linear model
- Binary variables: binary logistic regression
- Ordinal variables: ordinal logistic regression
- Repeated measurements (at 2 or more visits): generalised estimating equations

The significance level is 5%. 95% CI will be provided for estimates.

7.1 Primary outcome and primary analysis

The primary outcome measure is time to all-cause death or hospitalisation, whatever occurs first. As an exception, elective hospitalisations for definitely non-cardiac reason will not be counted as an event. The adjudication is made by the CEC. Only events as adjudicated by the CEC will be included into primary analysis.

**Deviation from the study protocol:** The protocol contains the statement that hospitalisations not considered as events will be counted as censoring. This phrasing was made obviously in error. Such hospitalisations will simply be neglected as if they would not have occurred.

Time to event is calculated from the date of informed consent on the CRF page R and the date of death or admission to the hospital, whatever is relevant. If no event occurred, the date of the last documented study contact with the patient is the date of censoring.

Primary analysis is done by Cox regression with the randomised group as factor and the co-variables used for stratification of the randomisation as specified on CRF page R: age<70 years (yes/no), sex, PHQ sum score (9-16 vs. 17-27), outpatient (yes/no).

**Deviation from the study protocol:** The protocol specifies the log-rank test for Kaplan-Meier estimates as primary test. Since the contemporary points to consider in statistical analysis require adjusting for stratification variables in primary analysis, we shall do so, too. Cox regression is then more suitable since the stratified log-rank test is associated with loss of power, particularly when stratifying by multiple factors.

7.2 Secondary analyses of the primary outcome

The following additional analyses will be carried out for the primary outcome:
• Unstratified Kaplan-Meier analysis (incidence curves + log-rank test)
• Simple Cox regression with randomised group as the only factor
• Multiple Cox regression with the following predictor variables: treatment, sex, age, NYHA class, LV ejection fraction, baseline MADRS, diabetes, coronary artery disease, eGFR, haemoglobin, NTproBNP (log scale)
• Primary analysis using the OSM set only

7.3 Secondary time-to-event outcomes

The following endpoints will be analysed for differences between randomised groups:

• Unadjudicated death or first hospitalisation (in both ITT and OSM set)
• Death
• Cardiovascular death
• First hospitalisation (adjudicated and unadjudicated)
• First cardiovascular hospitalisation (adjudicated and unadjudicated)
• First HF hospitalisation (adjudicated and unadjudicated)
• Cardiovascular death or first HF hospitalisation (adjudicated and unadjudicated)
• Death or hospitalisation due to stroke (adjudicated and unadjudicated)

Ordinal regression analysis, adjusted for time in study, will be carried out for the number of hospitalisations (any, cardiovascular, HF; adjudicated and unadjudicated).

7.4 Depression outcomes

Comparisons of treatment groups, each adjusted for the respective baseline values, will be carried out for the following variables:

• Major secondary outcome: MADRS sum score at 12 weeks (ITT)
• MADRS sum score at 6 and 12 weeks (ITT)
• Same analysis with OSM set
• MADRS sum score at all visits
• PHQ-9 sum score at 6 and 12 weeks
• PHQ-9 sum score at all visits
7.5  **HF outcomes**

Comparisons of treatment groups, each adjusted for the respective baseline values, will be carried out for the following variables at all follow-up visits when data were recorded:

- NYHA class
- LV ejection fraction
- LV end-diastolic diameter
- Systolic tricuspid valve gradient
- Six minute walk distance (6MWD)
- NTproBNP

7.6  **Quality of life outcomes**

Comparisons of treatment groups, each adjusted for the respective baseline values, will be carried out for the following variables at all follow-up visits when data were recorded:

- **Major quality of life outcome**: SF-36 physical functioning scale
- All other scales of the SF-36
- KCCQ Clinical summary scale and Functional Status summary scale
- GAD-7 sum score
- MMSE sum score

7.7  **Relationship between depression and HF**

Longitudinal relationships between depression and HF will be analysed by generalised estimating equations (GEE). Depressive symptoms of the current and the preceding visit will be used to predict HF at the current visit. Vice versa, HF severity at the current and the preceding visit will be used to predict current depressive symptoms.

Several analyses should be carried out, using as HF severity variable

- NYHA class
- NT-proBNP level
- 6MWD

and as depressive symptom variable
• MADRS sum score
• PHQ-9 sum score

and as anxiety variable
• PHQ-GAD 7 score

7.8 Subgroup analyses

Subgroup analyses will be performed for the primary endpoint.

The method is Cox regression with randomised group and the subgroup variable, including the interaction term of both.

The following subgroup variables will be considered:

• Age
• Sex
• NYHA class at baseline (II vs. III-IV)
• Baseline NTproBNP
• Baseline heart rate
• Baseline LVEF
• Baseline left-ventricular end-diastolic diameter
• Heart failure aetiology (ischaemic versus other)
• History of depression (yes/no), if the yes subgroup is large enough
• Baseline MADRS sum score
• Baseline PHQ-9 sum score
• Baseline PHQ-GAD-7 sum score
• Baseline MMSE sum score

For quantitative subgroup variables, the subgroups >median and ≤median will be analyzed. Exploratory analyses by tertile subgroups should be added when non-monotonous effects might be suspected.
7.9 Compliance

This section should include:

- Comparison of randomised groups with respect to study medication dose (ordinal)
- Comparison of randomised groups with respect to changes in treatment with ACE inhibitors / AT1 receptor blockers (ACEI/ARB) and beta-blockers (BB) as % of recommended target dose
- Analysis of relationship between study medication and ACEI/ARB and BB treatment
- Analysis of relationship between depressive symptoms (MADRS and PHQ-9 sum scores) and ACEI/ARB and BB treatment
- Escitalopram plasma levels in the verum group
- Analysis of relationship of escitalopram plasma levels and depressive symptoms

Analyses will be done by GEE.
7.10  **Function of sympathetic nervous system outcomes**

This analysis is considered exploratory. Final specification will be subject to an amendment. The following measurements from long-time ECG and laboratory measurements will be considered for evaluation (at multiple follow-ups when available):

- mean heart rate
- heart rate variability
  - short term
  - long term
- arrhythmias
  - number and severity of complex ventricular arrhythmias (≥ couplets, number of triplets and VT / 24 hrs)
  - supraventricular arrhythmias including AF
- plasma cortisol
- urine norepinehrine excretion
- plasma aldosterone
- hs Troponin

7.11  **Systemic inflammation / endothelial function outcomes**

This analysis is considered exploratory. Final specification will be subject to an amendment. The following measurements will be considered for evaluation (at multiple follow-ups when available):

- CRP
- Fibrinogen
- uric acid
- IL-6
- IL-10
- TNF-α
7.12 Other biomarker outcomes

This analysis is considered exploratory. Final specification will be subject to an amendment. The following measurements will be considered for evaluation (at multiple follow-ups when available):

- platelet function parameters
- 24 hour catecholamine excretion
- cortisol diurnal rhythm (saliva)
8  SAFETY ANALYSIS

All safety analyses will be carried out in the ITT and the OSM sets.

8.1  Adverse events

The frequencies of adverse events (AE) according to the AE and SAE CRF pages in the randomised groups will be compared by Fisher’s exact test. The following categories will be reported:

- Each AE pre-specified by a code on the CRF
- For AEs specified by free text, frequent categories should be reported separately; all other events should be summarised as “other”.
- reasonable summaries of groups of AEs (e.g. cardiovascular)
- Total AEs
- Total SAEs

8.2  ECG data

This section describes the analyses of data documented in the ECG modules of the CRF sections V2 through V8.

The following parameters will be compared between treatment groups:

- QTc (Bazett) as the primary safety variable
- QTc (Fredericia)
- QRS time
- QT minus QRS time
- Heart rate

The method will be GEE, adjusting for the respective baseline value.

The following categorical variables will be compared between randomised by binary logistic regression, adjusting for the respective continuous baseline value and the number of measurements:

- QTc Bazett > 450 ms
- QTc Bazett > 470 ms
• QTc Fridericia > 450 ms
• QRS time > 120 ms

The following categorical variables derived from the long-term ECG will be also be compared:

• Mean heart rate / 24 h
• Mean number of complex ventricular arrhythmias (≥ couplets) / h
• Mean number of ventricular arrhythmias ≥ 3 consecutive VES (Triplets) / h
• Proportion of incident atrial fibrillation

## 8.3 Laboratory data

This section describes the analyses of data documented in the laboratory modules of the CRF sections V2 through V8. Quantities should be reported in SI units.

The following parameters will be compared between treatment groups:

• eGFR (MDRD formula)
• Liver profile
• Glucose
• HbA1C
• Electrolytes
• Hemoglobin
• Leukocytes (total count)

The method will be GEE, adjusting for the respective baseline value.

The following categorical variables will be compared between randomised by binary logistic regression, adjusting for the respective continuous baseline value and the number of measurements:

• Incident eGFR < 60 / 45 / 30 mL/min/1.73m²

## 8.4 Combined safety information

If information regarding a certain safety issue (e.g., renal function) is contained in part on AE sheets and in part in measurement data, variables with the pooled information should be
computed (e.g., renal dysfunction reported as AE or drop of eGFR below 60 mL/min/1.73m²) and be evaluated as binary outcomes.

8.5 Safety subgroup analyses

Exploratory subgroup analyses as specified in 7.8 will also be performed for kidney, liver, inflammation and ECG parameters with a safety background.
9 SCREENING DATA

In order to better understand the possible selection of the study sample from the target population in the screening and inclusion process, evaluation of the screening PHQ-9 and the pre-inclusion SCID will be incorporated. The following issues will be analysed:

- Dependency of PHQ-9 sum score (first screening) on age, sex, NYHA class and history of depression (general linear model)

- Dependency of suspected any depression (PHQ-9 sum score ≥9), major depression (≥12) and severe major depression (≥17) on age, sex, NYHA class and history of depression (binary logistic regression)

- Positive predictive value of the PHQ-9 sum score for the diagnosis of depression according to SCID (raw probabilities for the thresholds of 9, 12 and 17, and logistic model)

- Comparison of the first screening data (data on the screening PHQ-9 sheet) of patients who were included into the randomised trial and subjects who did not attend any further step in the inclusion process
10 REFERENCES