

# Comparison of Bisoprolol and Carvedilol in elderly heart failure (HF) patients: a randomised, double-blind multicentre study

<b>Submission date</b> 07/09/2005	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 07/10/2005	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 21/12/2015	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**EudraCT/CTIS number**  
2004-000957-47

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
EudraCT # 2004-000957-47

# Study information

## Scientific Title

Comparison of Bisoprolol and Carvedilol in elderly heart failure (HF) patients: a randomised, double-blind multicentre study

## Acronym

CIBIS-ELD

## Study objectives

With bisoprolol, the target dose can be reached more frequently in heart failure patient than with carvedilol.

Please note that as of 15/01/2008 some changes have been made to this trial record. All changes can be seen in the relevant sections of the record, under the date 15/01/2008. Please also note that the anticipated end date of this trial has been extended to 30/06/2008. The previous end date of this was 30/10/2007.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Ethics approval received from:

1. Germany: Ethikkommission der Charité on the 13th June 2007 (Amendment 5) (ref: 125/2004)
2. Serbia: Ethics board of the University Hospital on the 31st March 2006 (ref: 6108/18)
3. Slovenia: The national medical ethics committee on the 2nd July 2007 (ref: KME 188/06/07)

## Study design

Randomised, multicentre controlled trial

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## Participant information sheet

## Health condition(s) or problem(s) studied

Chronic heart failure

## Interventions

Current intervention as of 15/01/2008:

Double-blind (bisoprolol versus carvedilol) tolerance-guided beta-blocker titration.

#### Dosages of study drugs:

The target dose for bisoprolol was set at 10 mg/d, for carvedilol at 25 mg twice daily (b.i.d.) and 50 mg b.i.d. for patients greater than 85 kg.

#### Up-titration:

The beta-blocker dose is increased to the target dose at fortnightly intervals. Dose titration differs according to the previous medication schedule of each patient. After the initial dose, therapy is commenced with either dose increment 1 or 2. Patients greater than 85 kg receive dose increment 5 after six or eight weeks. This increment indicates an increase in dosage in the carvedilol group only; in the bisoprolol group the increment is only technically treated like a dose increase for blinding purposes. The highest tolerated dose increment is maintained until the primary endpoint is reached (final visit in week 10 or 12). In instances of medication intolerance, patients are instructed not to reduce the dose without medical advice. The physician determines whether the intolerance is avoidable by changing the concomitant medication. If this not the case, the dose is reduced by one increment. A further up-titration is not attempted to minimise the risk of non-adherence by repeatedly provoking symptoms of intolerance. If up-titration is delayed (e.g. by adjusting concomitant medication) but the dose not reduced, it is desirable to attempt reaching the bisoprolol 10 mg target dose during subsequent treatment, even if it was not attained during the study treatment phase. After the 12-week therapy phase, the beta-blocker is not to be abruptly discontinued due to the exacerbation of sympathetic activity. Instead, a beta-blocker should be prescribed as standard treatment after study completion.

#### Previous intervention:

Dose titrated beta blocker therapy for 12 weeks - Bisoprolol versus Carvedilol

#### Intervention Type

Drug

#### Phase

Not Specified

#### Drug/device/biological/vaccine name(s)

Bisoprolol, carvedilol

#### Primary outcome measure

Current primary outcome measures as of 15/01/2008:

Tolerance (yes/no) of the study medication target dose as per cardiology guidelines. Tolerance (= yes) is defined when:

1. Dose titration was possible up to the target dose
2. The study medication dose was not reduced. It is irrelevant whether unscheduled T-visits took place if the titration aim was not affected
3. The target dose is to be taken at the time of last visit. This dose has remained stable for at least 10 days. Tolerance is ascertained (i.e. there is no reason for dose reduction and the patient did not reduce it independently either)

#### Previous primary outcome measures:

Tolerability, measured as individually achieved dose at end of titration.

#### Secondary outcome measures

Current secondary outcome measures as of 15/01/2008:

Correlation between the medication and the following secondary endpoints:

1. Time to treatment failure (TTF)
2. Dose increment attained (% of maximum) for long term treatment
3. Number of adverse events (AE) or serious adverse events (SAE) in total as well as itemised according to their relation to dose reduction/ discontinuation of treatment
4. Lung function (vital capacity [VC], forced expiratory volume in the first second [FEV1], peak expiratory flow [PEF] and maximal mid-expiratory flow [MEF50])
5. NYHA class
6. 6-minute walk test
7. Diastolic function (according to the American Society of Echocardiography [ASE]) and left ventricular function (fractional shortening and EF according to Simpson [looking at four chambers] from echocardiography before and after beta-blocker titration)
8. Quality of life, depression and physical well-being (measured with the following instruments: 36-item short form health survey [SF-36], Patient Health Questionnaire [PHQ-D] and KWB-16)
9. Heart rate at rest and under stress
10. Plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP) and BNP concentration
11. Alteration of total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) and triglycerides plasma concentration
12. Investigation of parameters for the current medical treatment of HF patients = 65 years old:
13. Frequency of beta-blocker, diuretic, angiotensin converting enzyme (ACE)-inhibitor or angiotensin receptor antagonist prescription
14. Qualitative and quantitative survey of other therapeutic actions
15. Hospitalisations
16. Days alive and days out of hospital

Previous secondary outcome measures:

1. Survey on current drug therapy in heart failure patients greater than or equal to 65 years
2. Number of adverse events (AE's)
3. Changes during titration phase in:
  - 3.1. Lung function parameters
  - 3.2. NYHA class/EF
  - 3.3. 6-minute walking test
  - 3.4. Quality of life
  - 3.5. Heart rate (rest/stress)
  - 3.6. N-Terminal pro-B-type Natriuretic Peptide (NT-pro-BNP)
  - 3.7. High density lipoprotein (HDL), low density lipoprotein (LDL), and total cholesterol

**Overall study start date**

01/03/2005

**Completion date**

30/06/2008

## **Eligibility**

**Key inclusion criteria**

Current inclusion criteria as of 15/01/2008:

1. Age greater than or equal to 65 years
2. Current diagnosis of chronic heart failure from New York Heart Association (NYHA) II - IV or ejection fraction (EF) less than 40%

3. Clinically stable heart failure for 2 weeks before inclusion
4. Informed consent

Previous inclusion criteria:

1. Age greater than or equal to 65 years
2. Chronic heart failure New York Heart Association (NYHA) II - IV or ejection fraction (EF) less than 40%
3. Clinically stable heart failure for 2 weeks before inclusion
4. Informed consent given

**Participant type(s)**

Patient

**Age group**

Senior

**Sex**

Both

**Target number of participants**

1040

**Key exclusion criteria**

Current exclusion criteria as of 15/01/2008:

Most relevant exclusion criteria:

1. Acute/decompensated HF
2. Shock, pulmonary embolism
3. Obstructive/restrictive cardiomyopathy
4. Severe pulmonary disorders/asthma
5. Inflammatory heart diseases
6. Standard exclusion criteria (as listed in the protocol)
7. Contraindications against beta blockers (as listed in the protocol)
8. Restricted concomittant medication (as listed in the protocol)

Previous exclusion criteria:

Most relevant exclusion criteria:

1. Acute/decompensated HF
2. Shock, pulmonary embolism
3. Obstructive/restrictive cardiomyopathy
4. Severe pulmonary disorders/asthma
5. HTN not controlled
6. Inflammatory heart diseases
7. Standard exclusion criteria (as listed in the protocol)
8. Contraindications against beta blockers (as listed in the protocol)
9. Restricted concomittant medication (as listed in the protocol)

**Date of first enrolment**

01/03/2005

**Date of final enrolment**

30/06/2008

# Locations

## Countries of recruitment

Germany

Montenegro

Serbia

Slovenia

## Study participating centre

Charite Campus Virchow Klinikum

Augustenburger Platz 1

Germany

13353

# Sponsor information

## Organisation

German Heart Failure Competence Network (Germany)

## Sponsor details

Charite Campus Virchow Klinikum

Department of Cardiology

Augustenburger Platz 1

Berlin

Germany

13353

## Sponsor type

Research organisation

## Website

<http://www.knhi.de>

# Funder(s)

## Funder type

Government

## Funder Name

## Funder Name

Merck Pharma GmbH (Germany) - drug supplies

## Results and Publications

### Publication and dissemination plan

Not provided at time of registration

### Intention to publish date

### Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Not provided at time of registration

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	protocol	01/09/2008		Yes	No
<a href="#">Results article</a>	results	01/06/2011		Yes	No
<a href="#">Results article</a>	results	10/02/2013		Yes	No
<a href="#">Results article</a>	results	01/06/2013		Yes	No
<a href="#">Results article</a>	results	01/02/2016		Yes	No