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

Submission date 07/09/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 07/10/2005	**Overall study status** Completed	
Last Edited 21/12/2015	**Condition category** Circulatory System	

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
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13353

Sponsor information

Organisation
German Heart Failure Competence Network (Germany)

Sponsor details
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Sponsor type
Research organisation

Website
http://www.knhi.de

Funder(s)

Funder type
Government

Funder Name

German Federal Ministry of Education and Research (Bundesministerium Für Bildung und Forschung [BMBF]) (Germany)

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?
Protocol article	protocol	01/09/2008		Yes	No
Results article	results	01/06/2011		Yes	No
Results article	results	10/02/2013		Yes	No
Results article	results	01/06/2013		Yes	No
Results article	results	01/02/2016		Yes	No