ISRCTN94726526 https://doi.org/10.1186/ISRCTN94726526

Aldosterone receptor blockade in Diastolic Heart Failure: a double-blind, randomised, placebo-controlled, parallel group study to determine the effects of spironolactone on exercise capacity and diastolic function in patients with symptomatic diastolic heart failure

Submission date 10/10/2006	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 07/11/2006	**Overall study status** Completed	
Last Edited 06/04/2023	**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

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Aldosterone receptor blockade in Diastolic Heart Failure: a double-blind, randomised, placebo-controlled, parallel group study to determine the effects of spironolactone on exercise capacity and diastolic function in patients with symptomatic diastolic heart failure

Acronym
Aldo-DHF

Study objectives
The primary objective of this study is to determine in subjects with diastolic heart failure whether spironolactone is superior to placebo in improving maximal exercise capacity and diastolic heart function. Secondary objectives of this study are to determine in subjects with diastolic heart failure whether spironolactone is superior to placebo in improving several other measures of exercise capacity and diastolic function, as well as quality of life, neuroendocrine activation, morbidity and mortality. The study will also investigate clinical safety aspects.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Local ethics committee in Göttingen and the BfAM.

Study design
Multicenter, prospective, randomised, double-blinded, placebo-controlled, parallel group, phase IIb trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Diastolic heart failure

Interventions
Once randomised, all patients will take study medication (25 mg spironolactone or placebo) once daily in the morning for 12 months. Patients recruited in the first six months will be followed up to 18 months. Spironolactone will be applied in one fixed dose, i.e., 25 mg, but may be down titrated if indicated.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome measure
1. Change in maximum exercise capacity (peak VO2 on spiroergometry) at 12 months compared to baseline
2. Change in E/E´ (relation peak early transmitral ventricular filling velocity/early diastolic tissue Doppler velocity) as indicator of Left Ventricular End Diastolic Pressure (LVEDP) at 12 months

Secondary outcome measures
1. Change in primary endpoints at 18 months
2. Change in the echocardiographic Grade of diastolic dysfunction
3. Change in neuroendocrine activation (natriuretic peptides)
4. Change in six minutes walking distance
5. Change in quality of life (Minnesota living with heart failure questionnaire; Short Form Health Survey [SF-36])
6. Combined and separately morbidity and mortality (all-cause; cardiovascular)

Overall study start date
01/11/2006

Completion date
31/10/2008

Eligibility

Key inclusion criteria
1. Current heart failure symptoms consistent with New York Heart Association (NYHA) grade II or beyond
2. Left Ventricular Ejection Fraction (LVEF) more than or equal to 50% at rest
3. Sinus rhythm
4. Echocardiographic parameters of diastolic dysfunction (more than or equal to Grade I)
5. Peak Oxygen uptake (VO2) less than or equal to 20 ml/kg/min
6. Males and females of age 50 years or over
7. Written informed consent of the patient

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
420

Total final enrolment
422

Key exclusion criteria
1. Definite or probable pulmonary disease (Vital Capacity [VC] less than 80% or Forced Expiratory Volume in one second [FEV1] less than 80% of reference values on spirometry)
2. Severe obesity (Body Mass Index [BMI] more than or equal to 36 kg/m^2)
3. Psychological disorders with suspected interaction to study outcome
4. Prior documented intolerance to an aldosterone receptor antagonist
5. Prior documented systolic heart failure (LVEF less than or equal to 40%)
6. Changes in concomitant medication within the last two weeks prior screening visit
7. Significant coronary artery disease (current angina pectoris or ischemia on stress tests; untreated coronary stenosis more than 50%; Myocardial infarction or Coronary Artery Bypass Graft (CAGB) within the last three months)
8. Known contraindications for spironolactone
9. Significant laboratory abnormalities (potassium more than or equal to 5.1 mmol/L; haemoglobin less than or equal to 11g/dL, hematocrit less than or equal to 33%)
10. Significant renal dysfunction (creatinine more than 1.8 mg/dL)
11. Concomitant therapy with a potassium-sparing diuretic (e.g., triamterene, amiloride), potassium substitution, or high-dose acetylsalicylic acid (more than 500 mg/d) or permanent intake of non-steroidal antiphlogistic agents, digitalis
12. Insulin-dependent diabetes mellitus with a history of ketoacidosis
13. Suspected metabolic acidosis
14. Significant hypotension (blood pressure less than 90 mmHg systolic and/or less than 50 mmHg diastolic)
15. Any patient characteristic that may interfere with compliance with the study protocol, such as dementia, substance abuse, history of non-compliance with prescribed medications or medical appointments
16. Pregnant or nursing women
17. Women with child bearing potency without effective contraception (except for implants, injectables, combined oral contraceptives, some IntraUterine Devices [IUDs] or vasectomised partner)
18. Concomitant participation in other clinical trials
19. Therapy with an aldosterone receptor antagonist within the last three months
20. Participation in another clinical trial within the last 30 days

Date of first enrolment
01/11/2006

Date of final enrolment
31/10/2008

Locations

Countries of recruitment
Germany

Study participating centre
Department of Cardiology and Pneumology
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Sponsor information

Organisation
Georg-August University of Göttingen (Georg-August-Universität Göttingen) (Germany)

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Sponsor type
University/education

Website
http://www.uni-goettingen.de/

ROR
https://ror.org/01y9bpm73

Funder(s)

Funder type
Government

Funder Name
Federal Ministry for Education and Research (BMBF), Health Research (Germany)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	prototcol	01/08/2010		Yes	No
Results article	results	27/02/2013		Yes	No
Results article	results	30/11/2013		Yes	No
Results article	Post hoc analysis	19/10/2021	15/12/2021	Yes	No
Results article		04/09/2021	22/03/2022	Yes	No
Results article		05/04/2023	06/04/2023	Yes	No