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Effect of coadministration of ezetimibe with statin therapy versus statin therapy alone on flow mediated vasodilation in patients with coronary artery disease

Submission date
13/09/2008

Recruitment status
No longer recruiting

Registration date
17/09/2008

Overall study status
Completed

Last Edited
17/09/2008

Condition category
Circulatory System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title

Acronym
CEZAR

Study objectives
Atorvastatin 80 mg per day is more effective in the improvement of flow-mediated dilation of the right brachial artery than atorvastatin 10 mg plus ezetimibe 10 mg per day despite comparable reduction of plasma low-density lipoprotein (LDL) cholesterol concentration.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Ethics Committee of the Medical Association of Hamburg (Ethik-Kommission der Ärztekammer Hamburg), approved on 13/03/2003
2. State Medical Board of Registration in Rhineland-Palatinate (Landesärztekammer Rhineland-Palatinate), approved on 07/11/2005

Study design
Phase IV, double-blind, two-arm, parallel-group, randomised controlled trial (single-centre)

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Stable coronary artery disease

Interventions
Arm 1: Atorvastatin (oral) 80 mg per day for 8 weeks
Arm 2: Atorvastatin (oral) 10 mg + ezetimibe (oral) 10 mg per day for 8 weeks

Ultrasonic measurements of endothelial function were carried out at the beginning of treatment and at the end of the 8-week pharmacological intervention.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Ezetimibe and atorvastatin

Primary outcome(s)
Effect of treatment on the absolute change (in percentage) in flow-mediated dilation (FMD) at 8 weeks compared to baseline.

Key secondary outcome(s))
Effect of treatment, at 8 weeks compared to baseline, on the following:
1. Absolute change (in percentage) in nitroglycerin-mediated dilation (NMD)
2. Absolute change in LDL cholesterol plasma concentration
3. Absolute change in C-reactive protein plasma concentration
4. Absolute change in uric acid plasma concentration
5. Absolute change in 8-iso-prostaglandin F2 alpha urine concentration

Completion date
31/07/2006

Eligibility

Key inclusion criteria
1. Both males and females, over 18 years old
2. Angiographic, documented coronary heart disease with:
a. Generalized wall irregularities (stenosis <40%) and/or
b. Existence of at least one stenosis >50%
3. Endothelial dysfunction with flow-dependent dilation of the brachial artery of <6%
4. LDL cholesterol >100 mg/dl
5. Written consent of the patients for participation in the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Acute coronary syndrome
2. Stroke or peripheral revascularisation within 12 weeks before study enrolment
3. Known intolerance towards HMG CoA reductase inhibitors or ezetimibe
4. Clinically significant valvular disease
5. Hypertrophic obstructive cardiomyopathy
6. Sustained ventricular arrhythmias
7. Syncope within four weeks before the study
8. Severe respiratory disease
9. Unstable diabetes mellitus requiring frequent adjustments in insulin doses
10. Known hypothyroidism
11. Known hyperthyroidism
12. Gastrointestinal disorders (such as Crohn's disease), which could lead to decreased

absorption of the study drug
13. Chronic liver disease
14. History of pancreatitis
15. History of organ transplantation
16. Clinically significant heart failure with left ventricular ejection fraction of <30%
17. Symptoms of orthostatic hypotension, or a systolic blood pressure in the supine position of <90 mmHg
18. Systolic blood pressure >180 mmHg and/or diastolic blood pressure >105 mmHg despite antihypertensive therapy
19. Elevated serum creatinine of >2.0 mg/dL or known nephrotic syndrome
20. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >1.5 times above the upper normal limit
21. Triglyceride level >400 mg/dl
22. Treatment with an HMG CoA reductase inhibitor during the last three months
23. Treatment with ezetimibe during the last three months
24. Initiation of treatment with an angiotensin converting enzyme (ACE) inhibitor, AT1-receptor antagonist, or calcium channel blocker within the past four weeks
25. Treatment with fibrates or colestipol during the last three months
26. Current treatment with macrolide antibiotics, niacin or antimycotics of azole type
27. Expected problems with compliance or follow-up visits (no fixed residence, alcohol or drug abuse, history of failure of medical advice, psychiatric diseases, etc.)
28. For women: pregnancy, breast feeding or possible pregnancy (women of childbearing age on an acceptable method of contraception may be included)
29. Simultaneous participation in another study
30. Therapy with another investigational product within a period of 30 days before the study

Date of first enrolment
01/07/2003

Date of final enrolment
31/07/2006

Locations

Countries of recruitment
Germany

Study participating centre
Johannes Gutenberg-Universität Mainz
Mainz
Germany
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Sponsor information

Organisation

Johannes Gutenberg-University Mainz (Germany)

ROR
https://ror.org/023b0x485

Funder(s)

Funder type
University/education

Funder Name
University of Hamburg (Germany)

Funder Name
Johannes Gutenberg-University Mainz (Germany)

Alternative Name(s)
Johannes Gutenberg University of Mainz, University of Mainz, Johannes Gutenberg University Mainz, JGU

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration