PLEASE NOTE: *This trial has been registered retrospectively.*

Trial Description

Title

Randomized Controlled Trial of Simvastatin in Amnestic MCI Patients

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

A German multicenter clinical trial (SIMaMCI) investigates, if the risk of developing Alzheimer's disease can be lowered by intake of Simvastatin, a drug used to lower plasma cholesterol level. The study is sponsored by the Federal Ministry of Education and Research.
Apart from lowering cholesterol levels, Simvastatin presumably inhibits the production of beta-amyloid, a protein which is related closely to the development of Alzheimer's disease. Retrospective analyses showed, that patients who have taken Statins, developed less frequently dementia.
Clinical lead is Prof. Isabella Heuser, Head of the Department of Psychiatry and Psychotherapy at the Charité, Berlin.
Worldwide, this is the first placebo-controlled, double-blinded prevention trial. In total 640 subjects will be included. Treatment with Simvastatin, resp. placebo will be offered for up to 5 years. Additionally, neuropsychological tests, blood and liquor tests, genetic analyses and MRI will be carried out, to monitor the success of the treatment and to investigate further the possible mechanisms of Statins in the prevention of Alzheimer's disease.
To participate the following criteria have to be met:
1. Impaired objective memory function; 2. No current or previous use for more than 3 months of an approved, experimental or over-the-counter antidementia drug; 3. No Medical indication for treatment with a statin or intake of a statin for more than 6 weeks; 4. No severe cardiovascular or other diseases. 5. Presence of a spouse of close relative; 6. age 55 - 85

Brief Summary in Scientific Language

Probands with MCI are at high risk to develop Alzheimer´s dementia (AD). Simvastatin may lower the production of β-amyloid a hallmark of AD in the brain and may additionally reduce oxidative stress and inflammation as well as increase endothelial nitric oxide synthetase and improve endothelial function. Simvastatin crosses the blood brain barrier, effects phospholipid transfer protein activity and phospho-tau-181 levels. Simvastatin protects cortical neurons from excitotoxicity. Primary hypothesis: Simvastatin significantly reduces the conversion rate to

Alzheimer's disease in patients with MCI as compared to MCI patients receiving placebo
Secondary hypotheses (to be evaluated by means of exploratory statistical methods): (1) The benefit from simvastatin treatment is larger in patients with a low level of β-amyloid (Aβ42 530ng/l; Aβ40 5612 ng/l) / increased level of Tau (t-Tau 350 ng/l; p-Tau 60 ng/l) in CSF as compared to patients above/below the respective cut-off values. (2)The benefit from simvastatin treatment is larger in APO-E4 allele carriers than in other APO-E allele individuals

Organizational Data

- DRKS-ID: **DRKS00000440**
- Date of Registration in DRKS: **2010/06/07**
- Date of Registration in Partner Registry or other Primary Registry: **2009/02/11**
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **ZS EK 12 4725/08 , Ethik-Kommission des Landes Berlin**

Secondary IDs

- EudraCT-Number: **2008-002226-11**
- Primary Registry-ID: **NCT00842920 (ClinicalTrials.gov)**
- BfArM-No.: **4034563**

Health condition or Problem studied

- ICD10: **F06.7 - Mild cognitive disorder**

Interventions/Observational Groups

- Arm 1: **Simvastatin, 60 mg, once a day, oral**
- Arm 2: **placebo, once a day, oral**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **Double or multiple blind**

Study Type: **Interventional**

Study Type Non-Interventional: **[---]***

Allocation: **Randomized controlled trial**

Blinding: **Double or multiple blind**

- Who is blinded: **[---]***
- Control: **Placebo**
- Purpose: **Prevention**
- Assignment: **Parallel**
- Phase: **IV**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

Length of conversion-free interval, staring at the time of randomization, with conversion being defined as an increase of the CDR score beyond 0.5

Secondary Outcome

1. Change in ADAS-cog and FCSRT score; 2. Change in CDR sum of boxes; 3. Change in ADCS-ADL score; 4. Change in volumetric brain measures; 5. Change in CSF and blood measures of ß-amyloid peptides, total and phosphorylized TAU proteins and measures of cerebral cholesterol metabolites; 6. Impact on cost efficacy ratio (ICER); 7. Pharmacogenetic prediction parameters

Countries of recruitment

- DE **Germany**

Locations of Recruitment

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2009/01/09**
- Target Sample Size: **640**
- Monocenter/Multicenter trial: **Multicenter trial**
-

Planned/Actual: **Actual**

(Anticipated or Actual) Date of First Enrollment: **2009/01/09**

Target Sample Size: **640**

Monocenter/Multicenter trial: **Multicenter trial**

National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **55 Years**
- Maximum Age: **85 Years**

Additional Inclusion Criteria

(1) Self and informant report of gradually increasing memory impairment for at least six months.
(2) Objective memory impairment
(3) Intact basic activities of daily living
(4) Preserved general cognitive function, not demented
(5) Absence of a detectable cause of memory disorder
(6) Age 55 to 85.
(7) Females without childbearing potential
(8) A total cholesterol ≥90 mg/dl
(9) LDL-cholesterol <130 mg/dl. LDL-cholesterol 130-160 mg/dl ≤ 3 risk factors including age or 160-190 mg/dl and 2 risk factors (only controlled hypertension and age)
(10) Informed consent (according AMG §40 (1) 3b)
(11) No participation in other clinical trials 2 months before and after participation in this study

Exclusion criteria

(1) Hypersensitivity against Simvastatin, active liver disease or lasting increase of serum transaminases for unclear reason
(2) Unstable medical, neurological or psychiatric disease
(3) Lack of a spouse or a close relative
(4) Use of a registered anti-dementia drug or a nootropic
(5) Chronic use of anti-inflammatory drugs
(6) History of stroke, coronary heart disease or myocardial infarction. Severe renal insuffiency.
(7) LDL-cholesterol 130-160 mg/dl and > 3 risk factors or 160-190 mg/dl and > 2 risk factors including age. LDL-cholesterol >190 mg/dl
(8) Comedication with Diltiazem, Verapamil, Amiodaron, Itraconazol, Ketokonazol, Erythromycin,Clarithromycin, Telithromycin, Ciclosporin, Gemfibrozil,Nefazodon, HIV-protease inhibitors, Benzodiazepines,
Tricyclic antipsychotics or other anticholinergic drugs;Comedication of other statins.
(9) Persons who are detained officially or legally to an official institute

Addresses

■ **Primary Sponsor**

Charité Universitätsmedizin Berlin
Charitéplatz 1
10117 Berlin
Germany

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

■ **Contact for Scientific Queries**

Klinik für Psychiatrie und Psychotherapie, Charité - Universitätsmedizin Berlin CBF
Mr. Dr. med. Oliver Peters
Eschenallee 3
14050 Berlin
Germany

Telephone: **[---]***
Fax: **[---]***
E-mail: **oliver.peters at charite.de**
URL: **http://www.charite-psychiatrie.de/nc/main/module/psychiatriedesalterns.html**

■ **Contact for Public Queries**

Klinik für Psychiatrie und Psychotherapie, Charité -Universitätsmedizin CBF
Ms. Dr. rer. nat. Brigitte Haas
Eschenallee 3
14050 Berlin
Germany

Telephone: **+49-30-8445-8392**
Fax: **+49-30-8445-8350**
E-mail: **brigitte.haas at charite.de**
URL: **http://www.charite-psychiatrie.de/nc/main/module/psychiatriedesalterns.html**

Sources of Monetary or Material Support

■ **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

Bundesministerium für Bildung und Forschung - BMBF

Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)

Dienstsitz Berlin

Hannoversche Straße 28-30
10115 Berlin
Germany

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*