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Study of Heart And Renal Protection

Submission date 20/12/2004	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 31/01/2005	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 31/10/2019	**Condition category** Circulatory System	[_] Individual participant data

Plain English summary of protocol
http://www.ctsu.ox.ac.uk/~sharp/QandA_background.htm

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT00125593

Clinical Trials Information System (CTIS)
2004-001156-37

Protocol serial number
CTSU SHARP 1

Study information

Scientific Title
A randomised controlled trial of ezetimibe and simvastatin versus placebo to reduce low density lipoprotein cholesterol in patients with chronic kidney disease

Acronym
SHARP

Study objectives
Reducing low density lipoprotein (LDL) cholesterol will reduce the risk of major vascular events in patients with chronic kidney disease and may delay progression to end-stage renal disease.

Protocol can be found at: http://www.ctsu.ox.ac.uk/~sharp/download_protocol_en_v5.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
Thames Valley MREC (Multicentre Research Ethics Committee), 25/04/2003, ref: 02/12/022

Primary study design
Interventional

Study design
Randomised controlled trial

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prevention of vascular disease in chronic kidney disease patients

Interventions
Following a 6-week run-in phase, participants are initially randomised to:
Arm 1: placebo, OR
Arm 2: ezetimibe 10 mg + simvastatin 20 mg daily, OR
Arm 3: simvastatin 20 mg daily (1 year only of treatment with simvastatin, then re-randomisation of Arm 3 participants to placebo [Arm 3a] or ezetimibe + simvastatin [Arm 3b]

Follow-up is scheduled to continue until all participants have been followed up for at least 4 years, regardless of whether they are continuing to take study treatment.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

Ezetimibe, simvastatin

Primary outcome(s)
Major vascular events (defined as non-fatal myocardial infarction or cardiac death, non-fatal or fatal stroke, or revascularisation) at end of study

Please note, in October 2009, the Steering Committee decided to change the primary outcome to major atherosclerotic events, defined as the combination of MI, coronary death, ischaemic stroke, or any revascularization procedure (ie, exclusion of non-coronary cardiac deaths and strokes confirmed to be haemorrhagic from the original major vascular event outcome). The independent sponsor (University of Oxford) was required by its contract with the main funder (Merck/Schering-Plough) to seek its formal agreement to any protocol change, but the funder declined to approve the changes agreed by the Steering Committee. Although it was therefore not possible to revise the protocol accordingly, the Steering Committee was free to change the statistical analysis plan as it considered appropriate whilst it remained blind to the effects of treatment on efficacy end points. The 'key outcome' was therefore changed to 'Major Atherosclerotic Events' by the Steering Committee whilst still blind to the effects of treatment on clinical outcomes. This is described in the following paper: SHARP Collaborative Group. Study of Heart and Real Protection (SHARP): Randomized trial to assess the effects of lowering low-density lipoprotein cholesterol among 9,438 patients with chronic kidney disease. Am Heart J 2010; 160: 785-94 (http://www.ncbi.nlm.nih.gov/pubmed/21095263).

Key secondary outcome(s)
1. Major vascular events at end of study
2. Major cardiac events (non-fatal myocardial infarction [MI] or cardiac death) at end of study
3. Stroke (fatal or non-fatal) at end of study
4. Coronary or non-coronary revascularisation at end of study
5. Mortality, both overall and within particular categories at end of study
6. Hospital admission for angina at end of study
7. End-stage renal disease (need for long-term dialysis or transplantation) at end of study
8. End-stage renal disease or death from any cause at end of study

Completion date
02/09/2010

Eligibility

Key inclusion criteria
1. History of chronic kidney disease (CKD): either patients who are pre-dialysis (with a plasma or serum creatinine greater than or equal to 150 µ/l [greater than or equal to 1.7 mg/dl] in men, or greater than or equal to 130 µ/l [greater than or equal to 1.5 mg/dl] in women); or patients on dialysis (haemodialysis or peritoneal dialysis)
2. Men or women aged greater than or equal to 40 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Sex
All

Key exclusion criteria
1. Definite history of myocardial infarction or coronary revascularisation procedure
2. Functioning renal transplant, or living donor-related transplant planned
3. Less than 2 months since presentation as an acute uraemic emergency (but may be entered later, if appropriate)
4. Definite history of chronic liver disease, or abnormal liver function (i.e. alanine aminotransferase [ALT] >1.5 x upper limit of normal [ULN] or, if ALT not available, aspartate aminotransferase [AST] >1.5 x ULN). (Note: Patients with a history of hepatitis are eligible provided these limits are not exceeded).
5. Evidence of active inflammatory muscle disease (e.g. dermatomyositis, polymyositis), or creatine kinase (CK) >3 x ULN
6. Definite previous adverse reaction to a statin or to ezetimibe
7. Concurrent treatment with a contraindicated drug (Note: Patients who are temporarily taking such drugs may be re-screened for participation in the study when they discontinue them, if appropriate). These contraindicated drugs include:
a. HMG-CoA reductase inhibitor ('statin')
b. Fibric acid derivative ('fibrate')
c. Nicotinic acid
d. Macrolide antibiotic (erythromycin, clarithromycin)
e. Systemic use of imidazole or triazole antifungals (e.g. itraconazole, ketoconazole)
f. Protease-inhibitors (e.g. antiretroviral drugs for human immunodeficiency virus [HIV] infection)
g. Nefazodone
h. Ciclosporin
8. Child-bearing potential (i.e. premenopausal woman who is not using a reliable method of contraception)
9. Known to be poorly compliant with clinic visits or prescribed medication
10. Medical history that might limit the individual's ability to take trial treatments for the duration of the study (e.g. severe respiratory disease, history of cancer other than non-melanoma skin cancer, or recent history of alcohol or substance misuse)

Date of first enrolment
01/06/2003

Date of final enrolment
02/09/2010

Locations

Countries of recruitment
United Kingdom

England

Australia

Austria

Canada

China

Czech Republic

Denmark

Finland

France

Germany

Malaysia

Netherlands

New Zealand

Norway

Poland

Sweden

Thailand

United States of America

Study participating centre
CTSU
Oxford
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Sponsor information

Organisation
University of Oxford (UK)

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
Merck Schering-Plough (UK)

Results and Publications

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?
Results article	results	01/11/2010		Yes	No
Results article	results	25/06/2011		Yes	No
Results article	results	01/05/2017		Yes	No
Protocol article	protocol for 5-year follow-up study	14/10/2019	31/10/2019	Yes	No
Basic results				No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes