

Effect of statins on functional regulation of endothelial nitric oxide synthase (eNOS) in heart failure

Submission date 19/09/2008	Recruitment status No longer recruiting	☒ Prospectively registered ☐ Protocol
Registration date 27/10/2008	Overall study status Completed	☐ Statistical analysis plan ☐ Results
Last Edited 09/06/2016	Condition category Circulatory System	☐ Individual participant data ☐ Record updated in last year

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

Dr Mark Harbinson

Contact details

Department of Therapeutics and Pharmacology
Whitla Medical Building
Lisburn Road
Belfast
United Kingdom
BT9 7BL

Additional identifiers

Protocol serial number

Sponsors ref: 07009GM-A

Study information

Scientific Title

Effect of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase inhibition on endothelial dysfunction, bioavailability of tetrahydrobiopterin (BH4) and functional regulation of endothelial nitric oxide synthase (eNOS) in human heart failure

Study objectives

Treatment with 3-hydroxy-3-methylglutaryl coenzyme A (HMG Co-A) reductase inhibitors in patients with heart failure will result in reduced uncoupling of endothelial nitric oxide synthase (eNOS), detected biochemically by increased production of nitric oxide and reduced production of free radicals and functionally by improved flow mediated dilatation of the brachial artery and changes in velocity time waveforms; and that these changes can be explained in part by detection of increased levels of tetrahydrobiopterin (BH4).

Ethics approval required

Old ethics approval format

Ethics approval(s)

Health and Social Care Research Ethics Committee 1, 28/10/2008, ref: 08/NIR01/74

Primary study design

Interventional

Study design

Parallel group double-blind randomised placebo-controlled trial

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Heart failure with systolic dysfunction

Interventions

Simvastatin 40 mg orally (or placebo) once a day (in the evening) will be administered for 6 weeks to each study participant.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Simvastatin

Primary outcome(s)

Changes in levels of superoxide, peroxynitrite, nitric oxide, tetrahydrobiopterin and brachial artery flow mediated dilatation and pulse contour analysis. Each outcome measure will be assessed at an initial visit, and then following randomisation and 6 weeks of treatment.

Key secondary outcome(s)

Changes in levels of markers of left ventricular (LV) dysfunction, adrenomedullin, N-terminal prohormone brain natriuretic peptide (NT proBNP) and intermedin. Each outcome measure will be assessed at an initial visit, and then following randomisation and 6 weeks of treatment.

Completion date

30/11/2011

Eligibility

Key inclusion criteria

1. Both males and females, over 18 years of age
2. Diagnosis of heart failure with an ejection fraction less than 35% determined by 2D echocardiography. Patients will be typically receiving maximal therapy for treatment of heart failure, including loop diuretics, angiotensin converting enzyme inhibitors or angiotensin receptor blockers, beta-blockers and spironolactone.
3. Patients must also be able to give informed consent, and to attend for follow up appointments

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

Key exclusion criteria

1. History of diabetes mellitus (fasting glucose greater than 7 mmol/L) or uncontrolled hypertension (blood pressure [BP] greater than 140/90 mmHg) or are receiving the thienopyridine derivative clopidogrel
2. Abnormal liver function (defined as aspartate aminotransferase [AST] or alanine aminotransferase [ALT] greater than three times upper limit of normal) or have had a previous documented adverse reaction to statin therapy or hypersensitivity to simvastatin or any of the excipients
3. Pregnant or lactating
4. Any patient who has an adverse reaction to statin therapy following initiation of treatment
5. Patients taking potent CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, human immunodeficiency virus [HIV] protease inhibitors, erythromycin, clarithromycin)
6. Patients taking cyclosporin, gemfibrozil or greater than 1 g/day niacin

Date of first enrolment

01/11/2008

Date of final enrolment

30/11/2011

Locations

Countries of recruitment

United Kingdom

Northern Ireland

Study participating centre

Department of Therapeutics and Pharmacology

Belfast

United Kingdom

BT9 7BL

Sponsor information

Organisation

Belfast Health and Social Care Trust (UK)

ROR

<https://ror.org/02tdmfk69>

Funder(s)

Funder type

Government

Funder Name

Research and Development Office of the Central Services Agency, Northern Ireland (UK) (ref: EAT/3719/07)

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?
HRA research summary			28/06/2023	No	No