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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	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 27/10/2008	**Overall study status** Completed	
Last Edited 09/06/2016	**Condition category** Circulatory System	

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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Study design
Parallel group double-blind randomised placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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 measure
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.

Secondary outcome measures
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.

Overall study start date
01/11/2008

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
60

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
Northern Ireland

United Kingdom

Study participating centre
Department of Therapeutics and Pharmacology
Belfast
United Kingdom
BT9 7BL

Sponsor information

Organisation
Belfast Health and Social Care Trust (UK)

Sponsor details
Postgraduate Office
Belfast City Hosptial
Lisburn Road
Belfast
Northern Ireland
United Kingdom
BT7 9AB

Sponsor type
Hospital/treatment centre

Website
http://www.belfasttrust.hscni.net

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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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