

Investigation of the anti-inflammatory effects of simvastatin in a human lipopolysaccharide induced model of acute lung injury

Submission date 29/04/2008	Recruitment status No longer recruiting	☐ Prospectively registered ☐ Protocol
Registration date 09/06/2008	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 30/06/2009	Condition category Respiratory	☐ Individual participant data

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

Dr Danny McAuley

Contact details

Intensive Care Unit
Royal Victoria Hospital
Grosvenor Road
Belfast
United Kingdom
BT12 6BA

Additional identifiers

Protocol serial number

060778SE-A

Study information

Scientific Title

Study objectives

Treatment with a clinically relevant dose of simvastatin will reduce pulmonary inflammation induced by lipopolysaccharide (LPS) inhalation in humans.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Office for Research Ethics Committees Northern Ireland (ORECNI). Date of approval: 25/10/2006 (ref: 06/NIR02/91)

Study design

Prospective, randomised, double-blind, placebo-controlled trial.

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Acute lung injury (ALI)

Interventions

Subjects will be randomised to the following three arms:

Arm 1: Simvastatin 40 mg enterally for 4 days prior to inhalation of LPS

Arm 2: Simvastatin 80 mg enterally for 4 days prior to inhalation of LPS

Arm 3: Placebo enterally for 4 days prior to inhalation of LPS

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

simvastatin

Primary outcome(s)

Reduction in broncho alveolar lavage (BAL) Interleukin-8 (IL8) concentration at 6 hours

Key secondary outcome(s))

1. To investigate whether treatment with simvastatin will modulate the following:

1.1. Alveolar inflammatory response at 6 hours

1.2 Plasma inflammatory response at 24 hours

1.3. Alveolar matrix metalloproteinase activity at 6 hours

1.4. Intracellular signalling in the alveolar space at 6 hours

1.5. Indices of alveolar epithelial and endothelial function and injury at 6 hours

2. To determine the potential mechanisms by which simvastatin may be beneficial in ALI

Completion date

05/11/2009

Eligibility

Key inclusion criteria

Healthy subjects, both males and females

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Sex

All

Key exclusion criteria

1. Age <18 years
2. Creatinine kinase (CK) >5 times upper limit of normal
3. Known active liver disease
4. Alcohol abuse or abnormal liver function tests: transaminases > 3 times upper limit of normal
5. Renal impairment (calculated creatinine clearance less than 60 mL/minute)
6. History of asthma, known lactose intolerance
7. Participation in other trials within the past 30 days
8. Pregnancy, breast-feeding or women of childbearing potential not using adequate contraception;
9. Current treatment with statins
10. Known hypersensitivity to the study medication
11. Previous adverse reaction to statins
12. Concomitant use of fibrates or other lipid-lowering therapy
13. Concomitant use of itraconazole, ketoconazole, erythromycin, clarithromycin, telithromycin, HIV protease inhibitors, nefazodone, grapefruit juice, cyclosporine, danazol, amiodarone, verapamil or diltiazem
14. Consent declined

Date of first enrolment

02/08/2006

Date of final enrolment

05/11/2009

Locations

Countries of recruitment

United Kingdom

Northern Ireland

Study participating centre
Intensive Care Unit
Belfast
United Kingdom
BT12 6BA

Sponsor information

Organisation
Belfast Health and Social Care Trust (UK)

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

Funder(s)

Funder type
Government

Funder Name
Intensive Care Society, Young Investigator's Award (UK)

Funder Name
REVIVE (UK)

Funder Name
Northern Ireland Health and Social Services Central Services Agency (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	15/06/2009		Yes	No