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

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

Plain English summary of protocolNot provided at time of registration

Contact information

Type(s)

Scientific

Contact name

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Contact details

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers 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

Secondary study design

Randomised controlled trial

Study setting(s)

Not specified

Study type(s)

Treatment

Participant information sheet

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 measure

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

Secondary outcome measures

- 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

Overall study start date

02/08/2006

Completion date

05/11/2009

Eligibility

Key inclusion criteria

Healthy subjects, both males and females

Participant type(s)

Patient

Age group

Adult

Sex

Both

Target number of participants

30

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

Northern Ireland

United Kingdom

Study participating centre

Intensive Care Unit

Belfast United Kingdom BT12 6BA

Sponsor information

Organisation

Belfast Health and Social Care Trust (UK)

Sponsor details

51 Lisburn Road
Belfast
Northern Ireland
United Kingdom
BT9 7AB
+44 (0)28 90 329241
rosemary.mcveigh@belfasttrust.hscni.net

Sponsor type

Hospital/treatment centre

Website

http://www.belfasttrust.hscni.net

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

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?
Results article	results	15/06/2009		Yes	No