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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 [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 09/06/2008	**Overall study status** Completed	
Last Edited 30/06/2009	**Condition category** Respiratory	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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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)

Primary study design
Interventional

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

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