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Simvastatin and severe sepsis

Submission date 15/07/2005	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 01/09/2005	**Overall study status** Completed	
Last Edited 17/05/2017	**Condition category** Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Version 2

Study information

Scientific Title
Simvastatin and severe Sepsis: a randomised controlled Trial

Acronym
SimSepT

Study objectives
Administration of 40 mg simvastatin to patients with severe sepsis reduces plasma concentration of interleukin-6 (IL-6) compared with patients receiving placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration.

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Severe sepsis

Interventions
Patients will receive a single tablet of either simvastatin 40 mg or identical placebo daily for 7 days (removed from protocol as of 10/10/2007: or until discharge from intensive care, whichever occurs earlier). If the patient is able to swallow, the tablet will be given orally. Otherwise, it will be crushed, suspended in water and administered via any existing enteral feeding or gastric drainage tube. Patients who are unable to receive enteral medications within 24-hours of first organ dysfunction will not be eligible for entry into the trial. All other management decisions will be at the discretion of the treating physician.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Simvastatin

Primary outcome measure
The difference in plasma IL-6 concentration between simvastatin and placebo treated groups, on day 3 of treatment. Plasma IL-6 will be measured using a commercially available enzyme linked immunosorbent assay (ELISA) kit. This technique has been used in other recent studies and is familiar to research staff in the department.

Secondary outcome measures
Inflammatory markers
Change in:
1. IL-6 concentration from baseline on days 1, 3 and 7 of treatment
2. C-Reactive Protein (CRP) concentration from baseline on days 1, 3 and 7 of treatment
3. Neutrophil count from baseline on days 1, 3 and 7 of treatment
4. Procalcitonin concentration from baseline on days 1, 3, and 7 of treatment

Infective complications
1. Antibiotic-free days during intensive care unit (ICU) admission
2. Number of new/nosocomial infections defined using National Institutes of Health (NIH) definitions

Safety
1. Number of patients withdrawn due to suspected drug reaction
2. Number of patients withdrawn due to muscle complications (CK ≥five-times ULN, myalgia, myositis, myopathy)
3. Number of patients withdrawn due to elevated plasma aspartate levels
4. Difference in mean plasma CK between groups

Mortality
1. ICU mortality
2. 30-day mortality
3. Hospital mortality

Disease severity
1. SOFA scores days 1, 3 and 7
2. Length of stay
3. ICU length of stay
4. Hospital stay

Compliance/efficacy
1. Plasma low density lipoprotein (LDL) concentration
2. High density lipoprotein (HDL)/LDL ratio

Overall study start date
01/09/2005

Completion date
31/12/2007

Eligibility

Key inclusion criteria
Patients eligible for inclusion:
1. Those admitted to the Adult Intensive Care Unit at John Radcliffe Hospital, Royal Sussex County Hospital and the Royal Berkshire Hospital (last two centres added 10/10/2007)
2. Severe sepsis or develop severe sepsis whilst in intensive care

Patients must be randomised and receive the first dose of simvastatin within 24 hours of first organ dysfunction to be included in the study.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
104

Key exclusion criteria
Patients will be excluded from the trial if they:
1. Are receiving simvastatin or another statin prior to admission
2. Refuse consent or their relatives refuse assent
3. Are less than 16 years of age
4. Are included in another interventional study
5. Have a known adverse reaction to statins
6. Have an indication or contraindication to treatment with a statin, according to the treating physician
7. Are unable to receive enteral medications
8. Are receiving drugs known to interact with simvastatin
9. Have active liver disease
10. Have severe renal impairment (anuria) (removed from protocol as of 10/10/2007: creatinine >400 µmol.l^-1 or requirement for renal replacement therapy despite adequate haemodynamic resuscitation)
11. Are at high risk of rhabdomyolysis [multiple trauma, crush injuries, extensive burns, baseline creatinine kinase (CK) ≥five-times upper limit of normal (ULN)]
12. Have a history of known or suspected porphyria
13. Are unlikely to survive more than 24 hours
14. Are unable to speak English (or whose relatives are unable to speak English) and a suitable interpreter cannot be found

Date of first enrolment
01/09/2005

Date of final enrolment
31/12/2007

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Adult Intensive Care Unit
Oxford
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Sponsor information

Organisation
Oxford Radcliffe Hospitals NHS Trust (UK)

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03h2bh287

Funder(s)

Funder type
Charity

Funder Name
Moulton Charitable Trust (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