

Simvastatin and severe sepsis

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

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

Dr J Duncan Young

Contact details

Adult Intensive Care Unit
John Radcliffe Hospital
Headley Way
Oxford
United Kingdom
OX3 9DU
+44 1865 220621
duncan.young@nda.ox.ac.uk

Additional identifiers

Protocol serial number

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

Study type(s)

Treatment

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(s)

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.

Key secondary outcome(s))

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 $\geq$ 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

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

Healthy volunteers allowed

No

Age group

Adult

Sex

All

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 $>400 \mu\text{mol.l}^{-1}$ 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) $\geq$ 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**

United Kingdom

England

Study participating centre

Adult Intensive Care Unit

Oxford

United Kingdom

OX3 9DU

Sponsor information

Organisation

Oxford Radcliffe Hospitals NHS Trust (UK)

ROR

<https://ror.org/03h2bh287>

Funder(s)

Funder type

Charity

Funder Name

Moulton Charitable Trust (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration