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Modifying Delirium Using Simvastatin

Submission date	Recruitment status	[_] Prospectively registered
26/03/2013	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
26/03/2013	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
17/05/2018	Mental and Behavioural Disorders	

Plain English summary of protocol

Background and study aims
Many different circumstances, such as severe infection or an accident, may result in a person becoming critically ill. For reasons that are unclear, when people are critically ill, their brain function is often impaired – a condition of severe confusion called delirium. Delirium is common, affecting up to two out of every three patients in intensive care units (ICU), and results in a longer hospital stay and a higher risk of death. Importantly, after recovery from the initial illness, following delirium, patients frequently go on to experience the equivalent of a mild or accelerated dementia. There is no proven effective treatment for delirium. It is thought that delirium is often a result of inflammation in the brain. Simvastatin, usually used to reduce cholesterol, has been shown to have significant anti-inflammatory properties. The aim of this study is to test the effectiveness of simvastatin at reducing delirium in the critically ill.

Who can participate?
Patients aged over 18 requiring mechanical ventilation (a machine to support breathing) within 72 hours of admission to intensive care.

What does the study involve?
Patients will be randomly allocated to be given either simvastatin or a dummy drug (placebo). We will count the number of days a patient is delirious, how fast they recover and how well their brain functions at 6 months using a telephone questionnaire.

What are the possible benefits and risks of participating?
Simvastatin is a safe, well-tolerated drug. If simvastatin reduces delirium it would likely decrease ICU stay. Demand for ICU exceeds supply and a treatment that reduced use of ICU resources would result in increased availability of facilities for critically ill patients. The potential impact of an effective treatment for delirium is considerable.

Where is the study run from?
Watford General Hospital (UK)

When is the study starting and how long is it expected to run for?
February 2013 to January 2015

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Dr Valerie Page
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2012-003114-13

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
13988

Study information

Scientific Title
Hydroxymethylglutaryl-CoA reductase inhibition with simvastatin in mechanically ventilated patients at high risk of delirium: a randomised double-blind placebo controlled trial

Acronym
MoDUS

Study objectives
Delirium is common affecting up to 2 out of every 3 patients in ICU, and results in a longer hospital stay and a higher risk of death. Importantly, after recovery from the initial illness, following delirium, patients frequently go on to experience the equivalent of a mild or accelerated 'dementia'. There is no proven effective treatment for delirium. It is thought that delirium is often a result of inflammation in the brain. Simvastatin, usually used to reduce

cholesterol, has been shown to have significant anti-inflammatory properties. This study is a randomised, double-blind, placebo controlled trial. 142 patients will randomly allocated to be given either simvastatin or a placebo. Outcomes include number of days a patient is delirious, how fast they recover and cognitive function at 6 months using an approved telephone questionnaire. If simvastatin reduces delirium it would likely decrease ICU stay. Demand for ICU exceeds supply and a treatment that reduced use of ICU resources would result in increased availability to appropriate facilities for critically ill patients. This study is being funded by a Research for Patients Benefit Grant and run in partnership with ICUSteps and the Alzheimer's Society.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North East - Newcastle & North Tyneside 1, 06/12/2012, ref: 12/NE/0383

Study design
Randomised double-blind placebo-controlled trial, Design type: Prevention, Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Generic Health Relevance and Cross Cutting Themes; Subtopic: Generic Health Relevance (all Subtopics); Disease: Critical Care

Interventions
Simvastatin 80 mg or placebo daily for up to 28 days

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Alive, delirium free and coma free days; Timepoint(s): 14 days

Secondary outcome measures
1. Incidence of delirium
2. Delirium/coma free days in first 28 days
3. Number of ventilator free days at 28 days
4. Length of critical care and hospital stay
5. Mortality at 6 months; (f) Organ failure free days
6. Cognitive Impairment at 6 months
7. Health related quality of life over the 6 month study period using the EQ-5D-5L
8. Quality adjusted life years at 6 months
9. Healthcare resource use and associated costs over the 6 month study period
10. Cost-effectiveness of the intervention at 6 months post-randomisation

Overall study start date
02/02/2013

Completion date
31/01/2015

Eligibility

Key inclusion criteria
1. Patients requiring mechanical ventilation within 72 hours of admission to intensive care.
2. Male & Female ; Lower Age Limit 18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 142; UK Sample Size: 142; Description: Intensive Care Patients

Key exclusion criteria
1. Age less than 18 years
2. Patient known to be pregnant
3. Known allergy to statin drugs
4. CK > 10 times upper limit of normal range
5. Alanine aminotransferase (ALT) >8 times the upper limit of normal range
6. Patients currently receiving ongoing and sustained treatment with any of the following; itraconazole, ketoconazole, HIV protease inhibitors, nefazodone, cyclosporine, amiodarone,

verapamil or diltiazem
7. Uncomplicated elective surgery
8. Patient expected to be discharged within 48 hours of admission
9. Patients with severe renal impairment (estimated creatinine clearance less than 30ml/minute) not receiving renal replacement therapy
10. Severe liver disease
11. Current or recent treatment (within 2 weeks) with statins
12. Physician decision that a statin is required for proven indication
13. Contraindication to enteral drug administration, e.g. patients with mechanical bowel obstruction. Patients with high gastric aspirates due to an ileus are not excluded.
14. Known participation in investigational medicinal product (IMP) trials within 30 days
15. Consent declined
16. Treatment withdrawal likely within 48 hours
17. Non-English speaking patients or those who do not adequately understand verbal or written information

Date of first enrolment
02/02/2013

Date of final enrolment
31/01/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
West Hertfordshire Hospitals NHS Trust
Watford
United Kingdom
WD18 0HB

Sponsor information

Organisation
West Hertfordshire Hospitals NHS Trust (UK)

Sponsor details
60 Vicarage Road
Watford
England
United Kingdom
WD18 0HB

Sponsor type
Hospital/treatment centre

Website
http://www.westhertshospitals.nhs.uk/

ROR
https://ror.org/03e4g1593

Funder(s)

Funder type
Government

Funder Name
NIHR (UK) - Research for Patient Benefit (RfPB); Grant Codes: PB-PG-0211-24123

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?
Protocol article	protocol	16/05/2015		Yes	No
Results article	results	01/09/2017		Yes	No
HRA research summary			28/06/2023	No	No