ISRCTN45190901 https://doi.org/10.1186/ISRCTN45190901

Collaborative H1N1 Adjuvant Treatment pilot trial

Submission date	Recruitment status	[_] Prospectively registered
23/02/2010	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
08/03/2010	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
08/03/2019	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr John Marshall

Contact details
St. Michael's Hospital
30 Bond Street
Toronto
Canada
M5B 1W8
+1 416 864 6060 ext. 5225
MarshallJ@smh.toronto.on.ca

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT01033955

Secondary identifying numbers
102785

Study information

Scientific Title
A double-blind placebo-controlled randomised pilot trial of the utility of statins as an adjuvant anti-inflammatory treatment in critically ill adults with suspected, probable or confirmed H1N1

Acronym
CHAT

Study objectives
Data from both observational studies in humans and interventional studies in animals suggest that the course of influenza can be favourably influenced by agents that are not classically considered to be treatments for influenza. As many of these treatments are inexpensive and readily available, and because they may provide independent benefit in viral infection, they are attractive adjuvant treatments for patients around the world, and ideally suited to use during a global pandemic. Our focus will be on the potential utility of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase inhibitors (statins) as an adjuvant anti-inflammatory treatment in critically ill adults with suspected, probable or confirmed H1N1 based on theoretical potential for benefit and promising experimental studies.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. St Michael's Hospital Research Ethics Office approved on the 23rd December 2009 (ref: 09-314)
2. Comite d'ethique de la recherche de l'institut universitaire de cardiologie et de pneumologie de Quebec approved on the 2nd February 2010 (ref: HL-4610)
3. King Abdulaziz University Hospital Biomedical and Research Committee approved 30th January 2010 (ref: 340-10)

All other centres will seek ethics approval before recruiting participants.

Study design
Double blind placebo controlled pilot randomised trial

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 below to request a patient information sheet

Health condition(s) or problem(s) studied
Critically ill influenza A/H1N1 infection

Interventions
Please note that as of 29/11/10 the anticpated end date of this study has been extended from 30 /08/10 to 30/08/11. This trial is in the recruitment phase.

Experimental drug: Rosuvastatin (Crestor®) -
The first dose of encapsulated study drug (day 1) will be administered within 4 hours of randomisation as a loading dose of 40 mg. Thereafter, doses of 20 mg will be administered daily starting on the next calendar day at 10 pm (+/- 4 hours) as a maintenance dose from days 2 to 14. If the patient is of Asian descent, is aged less than 18 years, or serum creatinine is greater than or equal to 248 µmol/L (2.8 mg/dL) dose adjustments will be made according to a dose adjustment algorithm.

Placebo Comparator -
An identical appearing placebo will be administered to patients in the second study arm and administered once daily through an enteral feeding tube or administered orally if the patient is able to safely take oral medications.

Total duration of treatment: 14 days (both arms)
Total duration of follow-up: 90 days (both arms)

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Rosuvastatin (Crestor®)

Primary outcome measure
Proportion of eligible patients enrolled in the CHAT Pilot Trial. Feasibility for the pilot study will be assessed by metrics that reflect our capacity to ultimately recruit a representative sample of 1050 patients in the planned full CHAT trial. We will consider the study to be feasible if we recruit at least 30% (commonly used threshold in ICU studies) of all eligible patients in participating ICUs through careful review of site screening logs.

Secondary outcome measures
1. Adherence to the medication administration regimen as outlined in the study protocol
2. Proportion of completed primary and secondary endpoints for the planned full CHAT trial that are collected
3. The number of patients who receive open-label statins
4. The number of consent withdrawals
5. Recruitment rates by approved consent model

All outcomes will be measured upon termination of this pilot study. However, adherence to medication administration will be recorded daily on study days 1 through 14 for each study subject.

Overall study start date
01/01/2010

Completion date
30/08/2011

Eligibility

Key inclusion criteria
1. Critically ill adult patients greater than 16 years of age (either sex) admitted to an adult intensive care unit (ICU) for any reason with suspected, probable or confirmed novel swine origin influenza A/H1N1 infection
2. Requiring mechanical ventilation (invasive or non-invasive)
3. Receiving antiviral therapy (any medication at any dose and for any intended duration) for less than 72 hours
4. Attending physician or intensivist must have a 'moderate' to 'high' index of suspicion for H1N1

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
80

Key exclusion criteria
1. Aged less than 16 years
2. Do not resuscitate or re-intubate order documented on chart or anticipated withdrawal of life support
3. Weight less than 40 kg
4. Unable to receive or unlikely to absorb enteral study drug (e.g. incomplete or complete bowel obstruction, intestinal ischaemia, infarction, short bowel syndrome)
5. Rosuvastatin specific exclusions:
5.1. Already receiving a statin (atorvastatin, lovastatin, simvastatin, pravastatin, rosuvastatin)
5.2. Allergy or intolerance to statins
5.3. Receiving niacin, fenofibrate, cyclosporine, gemfibrozil, any protease inhibitor (including but not limited to lopinavir, ritonavir) or planned use of oral contraceptives or estrogen therapy during the Intensive Care Unit (ICU) stay
5.4. Creatine kinase (CK) exceeds 5,000 U/L or alanine aminotransferase (ALT) exceeds 8 times the upper limit of normal (ULN)
6. Severe chronic liver disease (Child-Pugh Score 11 - 15)

7. Previous enrolment in this trial
8. Pregnancy or breast feeding
9. At the time of enrolment, receipt of greater than 72 hours of antiviral therapy
10. Known or suspected clinically significant myositis or myopathy

Date of first enrolment
01/01/2010

Date of final enrolment
30/08/2011

Locations

Countries of recruitment
Argentina

Australia

Canada

Mexico

New Zealand

Saudi Arabia

Study participating centre
St. Michael's Hospital
Toronto
Canada
M5B 1W8

Sponsor information

Organisation
St Michael's Hospital (UK)

Sponsor details
30 Bond Street
Toronto
Canada
M5B 1W8

Sponsor type
Hospital/treatment centre

Website
http://www.stmichaelshospital.com/

ROR
https://ror.org/04skqfp25

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (CIHR) (Canada) - http://www.cihr-irsc.gc.ca (ref: 102785)

Funder Name
Public Health Agency of Canada (PHAC) (Canada) (ref: 09-137443-391)

Funder Name
Physician's Services Incorporated (PSI) Foundation (Canada)

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	01/12/2011		Yes	No