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An efficacy and mechanism evaluation study of levosimendan for the prevention of acute organ dysfunction in sepsis

Submission date
18/09/2013

Recruitment status
No longer recruiting

Registration date
19/09/2013

Overall study status
Completed

Last Edited
11/01/2019

Condition category
Signs and Symptoms

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Septic shock is a condition where blood pressure falls in response to overwhelming infection, resulting in poor blood flow to the kidneys and other vital organs and leading to the failure of these organs. It is a life-threatening condition and requires emergency treatment in an intensive care unit. It is the commonest cause for admission to intensive care in the UK and despite improvements in its treatment around 40% of patients die as a result. It is normal practice for intensive care doctors to attempt to restore a patient's blood pressure to a relatively normal level using adrenaline-like drugs called catecholamines which can improve the function of the heart. However, it is increasingly being recognised that these drugs have important side effects and may even be associated with harm. Levosimendan is a new type of drug that improves the function of the heart in a different manner to the adrenaline-like drugs. It has been extensively studied in patients with heart failure and is a licensed drug for this group of patients in many European countries and elsewhere around the world. Around half of patients with septic shock may develop impaired heart function and associated kidney failure, and levosimendan has been shown to improve this. Its use in septicaemia (blood poisoning) has been studied in both animals and humans, and so far the small patient studies have shown promise, but none have been large enough to assess the effect on important patient-centred outcomes. The aim of this study to investigate whether levosimendan benefits patients with septicaemia by reducing the severity of organ failure.

Who can participate?
Patients aged 18 and over with septicaemia

What does the study involve?
Participants are randomly allocated to be infused with either levosimendan or a placebo (dummy drug) for 24 hours. Organ failure, kidney injury, heart output, duration of mechanical ventilation, and blood oxygen levels are assessed.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
ICU Charing Cross Hospital (UK)

When is the study starting and how long is it expected to run for?
November 2013 to October 2016

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

Who is the main contact?
Jonas Lexow
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2012-005159-18

Protocol serial number
15139

Study information

Scientific Title
An efficacy and mechanism evaluation study of Levosimendan for the Prevention of Acute oRgan Dysfunction in Sepsis (LeoPARDS)

Acronym
LeoPARDS

Study objectives

In this study we plan to undertake a randomised, controlled trial in a number of intensive care units to investigate whether levosimendan, when added to standard care, can produce important benefits for patients with septicaemia by reducing the severity of organ failure.

Ethics approval required
Old ethics approval format

Ethics approval(s)
First Medical Reasearch Ethic Committee (MREC), 26/04/2013; Ref: 13/LO/0365

Study design
Randomised; Interventional; Design type: Not specified, Treatment

Primary study design
Interventional

Study type(s)
Treatment

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
1. Levosimendan, 0.05 - 0.2 µg/kg/min infusion for 24 hours
2. Matching placebo, infusion for 24 hours
Follow Up Length: 6 month(s); Study Entry : Single Randomisation only

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Mean sequential organ failure assessment (SOFA) score; Timepoint(s): On ICU after randomisation

Key secondary outcome(s))
1. Acute kidney injury; Timepoint(s): Day 14
2. Cardiac output; Timepoint(s): upto 96 hours
3. Duration of mechanical ventilation; Timepoint(s): In ICU
4. Central venous oxygen saturation (ScvO2); Timepoint(s): upto 96 hours
5. Serum bilirubin; Timepoint(s): In ICU upto day 28

Completion date
31/10/2016

Eligibility

Key inclusion criteria
1. The target population includes adult patients (=18 years) who require vasopressor support for the management of sepsis despite fluid resuscitation
2. Inclusion criteria will use the internationally-established consensus definitions of sepsis. In brief, fulfil 2 out of 4 of the criteria of the systemic inflammatory response syndrome (SIRS) due to known or suspected infection within the previous 24 hours. The SIRS criteria are:
2.1. Fever (>38 C) or hypothermia (< 36 C)
2.2. Tachycardia (heart rate > 90 beats per minute)
2.3. Tachypnoea (respiratory rate > 20 breaths per minute or $PaCO_2$ < 4.3 kPa) or need for mechanical ventilation
2.4. Abnormal leukocyte count [> 12,000 cells/mm3, < 4000 cells/mm3, or > 10% immature (band) forms]
3. Hypotension, despite adequate intravenous fluid resuscitation, requiring treatment with a vasopressor infusion (e.g. noradrenaline/adrenaline/vasopressin analogue) for at least four hours and still having an ongoing vasopressor requirement at the time of randomisation.

Target Gender: Male & Female

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
The exclusion criteria are as follows:
1. More than 24 hours since meeting all the inclusion criteria
2. Endstage renal failure at presentation (previously dialysis-dependent)
3. Severe hepatic impairment (Child-Pugh class C)
4. A history of Torsades de Pointes
5. Significant mechanical obstructions affecting ventricular filling or outflow or both
6. Treatment limitation decision in place [e.g. Do not attempt resuscitation (DNAR) or not for ventilation/dialysis]
7. Known or estimated weight of more than135kg
8. Known to be pregnant
9. Previous treatment with levosimendan within 30 days
10. Known hypersensitivity to levosimendan or any of the excipients
11. Known to have received another investigational medicinal product within 30 days or currently in another interventional trial that might interact with the study drug.

Date of first enrolment
01/11/2013

Date of final enrolment
31/10/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
ICU Charing Cross Hospital
London
United Kingdom
W6 8RF

Sponsor information

Organisation
Imperial College of Science, Technology and Medicine (UK)

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research (NIHR) (UK); Grant Codes: 11/14/08

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

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	27/10/2016		Yes	No
Results article	results	01/11/2018		Yes	No
Protocol article	protocol	02/06/2014		Yes	No
HRA research summary			28/06/2023	No	No