

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

<b>Submission date</b> 18/09/2013	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 19/09/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 11/01/2019	<b>Condition category</b> Signs and Symptoms	<input type="checkbox"/> 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  
leopards@imperial.ac.uk

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Mr Jonas Lexow

**Contact details**  
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## Additional identifiers

**EudraCT/CTIS number**  
2012-005159-18

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
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 Research Ethics Committee (MREC), 26/04/2013; Ref: 13/LO/0365

### **Study design**

Randomised; Interventional; Design type: Not specified, 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 contact details to request a participant 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**

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 measure**

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

**Secondary outcome measures**

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 (ScvO<sub>2</sub>); Timepoint(s): upto 96 hours
5. Serum bilirubin; Timepoint(s): In ICU upto day 28

**Overall study start date**

01/11/2013

**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<sub>2</sub> < 4.3 kPa) or need for mechanical ventilation
  - 2.4. Abnormal leukocyte count [ $> 12,000$  cells/mm<sup>3</sup>,  $< 4000$  cells/mm<sup>3</sup>, 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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

Planned Sample Size: 516; UK Sample Size: 516; Description: Randomised 1:1

### **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 than 135kg
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**

England

United Kingdom

### **Study participating centre**

ICU Charing Cross Hospital

London

United Kingdom

W6 8RF

## **Sponsor information**

### **Organisation**

Imperial College of Science, Technology and Medicine (UK)

### **Sponsor details**

International Centre for Circulatory Health

Exhibition Rd

London

England  
United Kingdom  
SW7 2AZ

**Sponsor type**  
University/education

**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**

**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?
<a href="#">Protocol article</a>	protocol	02/06/2014		Yes	No
<a href="#">Results article</a>	results	27/10/2016		Yes	No
<a href="#">Results article</a>	results	01/11/2018		Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No