

# KARE - Keratinocyte growth factor in acute lung injury to reduce pulmonary dysfunction

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|--|---|---|
| <b>Submission date</b><br>06/09/2010   | <b>Recruitment status</b><br>No longer recruiting | <input type="checkbox"/> Prospectively registered<br><input checked="" type="checkbox"/> Protocol |
| <b>Registration date</b><br>23/09/2010 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>22/05/2017       | <b>Condition category</b><br>Respiratory          | <input type="checkbox"/> Individual participant data  |

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Prof Danny Francis McAuley

**Contact details**  
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United Kingdom  
BT12 6BN

## Additional identifiers

**EudraCT/CTIS number**  
2010-021186-70

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
10089DMCA-CS

# Study information

## Scientific Title

Keratinocyte growth factor in acute lung injury to reduce pulmonary dysfunction: a randomised placebo controlled trial

## Acronym

KARE

## Study objectives

The hypothesis is that treatment with palifermin will improve surrogate clinical outcomes in adult patients with acute lung injury and is safe.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Office for Research Ethics Committees Northern Ireland (ORECNI) HSC REC 2, 04/08/2010, ref: 10/NIR02/32

## Study design

Prospective randomised double-blind placebo-controlled phase II multi-centre 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 to request a patient information sheet

## Health condition(s) or problem(s) studied

Acute lung injury

## Interventions

Patients will be randomised to palifermin 60 µg/kg or normal saline placebo daily as a bolus intravenous injection for up to 6 days. Administration will not occur through an intravenous line that has been flushed with heparin. The intravenous line will be flushed with normal saline prior to and after study drug administration. The first dose of study drug will be administered within 4 hours of randomisation and subsequent doses will be at 10 am daily starting on the following calendar day.

## **Intervention Type**

Drug

## **Phase**

Phase II

## **Drug/device/biological/vaccine name(s)**

Palifermin

## **Primary outcome measure**

Oxygenation index (OI) at day 7 or the last available OI prior to patient discontinuation from the study. OI is a physiological index of the severity of ALI and measures both impaired oxygenation and the amount of mechanical ventilation delivered. We and others have shown OI is independently predictive of mortality in patients with ALI. We have chosen day 7 as we expect this time interval will minimise the competing effects of death and extubation, while allowing a sufficient time interval for a biological effect to occur.

OI is calculated as  $(\text{mean airway pressure [cm H}_2\text{O]} \times \text{FiO}_2 \times 100) = \text{PaO}_2 \text{ (kPa)}$ . These simple measurements are easily and routinely collected as part of standard ventilator practice.

## **Secondary outcome measures**

1. Oxygenation index (OI) at days 3 and 14
2. Physiological indices of acute lung injury, as measured by respiratory compliance (Cr<sub>s</sub>), P/F ratio, and the pulmonary dead space fraction at days 3, 7 and 14
3. Change in sequential organ failure assessment (SOFA) score from baseline to day 7 and 14
4. Safety and tolerability as assessed by the occurrence of AEs and Suspected Unexpected Serious Reactions (SUSARs)

Although the duration of ventilation and ICU stay as well as ICU and hospital mortality and 28-day mortality will also be documented, these important clinical outcomes are not included as major outcome measures as the study is not adequately powered to assess these outcomes.

## **Overall study start date**

10/09/2010

## **Completion date**

31/12/2013

# **Eligibility**

## **Key inclusion criteria**

Current inclusion criteria as of 23/01/2014:

1. Aged greater than 18 years, either sex
2. Acute lung injury (ALI) as defined by acute onset of:
  - 2.1. Hypoxic respiratory failure (partial pressure of oxygen in arterial blood [PaO<sub>2</sub>]/fraction of inspired oxygen [FiO<sub>2</sub>] less than or equal to 40 kPa)
  - 2.2. Bilateral infiltrates on chest X-ray consistent with pulmonary oedema
  - 2.3. No clinical evidence of left atrial hypertension or if measured, a pulmonary arterial occlusion pressure (PAOP) less than or equal to 18 mmHg
  - 2.4. Requirement for positive pressure mechanical ventilation via an endotracheal tube or

tracheostomy

All ALI criteria above must occur within the same 24-hour period. The onset of ALI is when the last ALI criterion is met. Patients must be enrolled within 72 hours of ALI onset.

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2. Acute lung injury (ALI) as defined by acute onset of:
  - 2.1. Hypoxic respiratory failure (partial pressure of oxygen in arterial blood [PaO<sub>2</sub>]/fraction of inspired oxygen [FiO<sub>2</sub>] less than or equal to 40 kPa)
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  - 2.4. Requirement for positive pressure mechanical ventilation via an endotracheal tube or tracheostomy

All ALI criteria above must occur within the same 24-hour period. The onset of ALI is when the last ALI criterion is met. Patients must be enrolled within 48 hours of ALI onset.

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Sex**

Both

### **Target number of participants**

60

### **Key exclusion criteria**

Current exclusion criteria as of 23/01/2014:

1. Aged less than 18 years
2. More than 48 hours from the onset of ALI
3. Pregnancy
4. Participation in a clinical trial of an investigational medicinal product within 30 days
5. Consent declined
6. Current treatment with KGF
7. Known hypersensitivity to palifermin or Escherichia coli derived proteins
8. Previous adverse reaction to palifermin
9. Active history of malignancy excluding haematological malignancies
10. Chronic liver disease with Child-Pugh score greater than 12

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3. Pregnancy
4. Participation in a clinical trial of an investigational medicinal product within 30 days
5. Consent declined

6. Current treatment with KGF
7. Patients with pancreatitis
8. Known hypersensitivity to palifermin or Escherichia coli derived proteins
9. Previous adverse reaction to palifermin
10. History of active malignancy
11. Chronic liver disease with Child-Pugh score greater than 12

**Date of first enrolment**

10/09/2010

**Date of final enrolment**

31/12/2013

## **Locations**

**Countries of recruitment**

Northern Ireland

United Kingdom

**Study participating centre**

**Royal Victoria Hospital**

Belfast

United Kingdom

BT12 6BN

## **Sponsor information**

**Organisation**

Belfast Health and Social Care Trust (UK)

**Sponsor details**

c/o Professor Ian Young

Trust Research Office

2nd Floor King Edward Building

Royal Victoria Hospitals

Grosvenor Road

Belfast

Northern Ireland

United Kingdom

BT12 6BA

**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.belfasttrust.hscni.net/>

**ROR**

<https://ror.org/02tdmfk69>

## Funder(s)

**Funder type**

Government

**Funder Name**

Public Health Agency for Northern Ireland (UK) - HSC Research and Development Division (ref: EAT/4208/09)

## 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 | 18/02/2013   |            | Yes            | No              |
| <a href="#">Results article</a>      | results  | 01/06/2017   |            | Yes            | No              |
| <a href="#">HRA research summary</a> |          |              | 28/06/2023 | No             | No              |