

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

Submission date 06/09/2010	Recruitment status No longer recruiting	☐ Prospectively registered ☒ Protocol
Registration date 23/09/2010	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 22/05/2017	Condition category Respiratory	☐ Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2010-021186-70

Protocol serial number
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

Primary study design

Interventional

Study design

Prospective randomised double-blind placebo-controlled phase II multi-centre trial

Study type(s)

Treatment

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(s)

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 (mean airway pressure [cm H₂O] x FiO₂ x 100) = PaO₂ (kPa). These simple measurements are easily and routinely collected as part of standard ventilator practice.

Key secondary outcome(s)

1. Oxygenation index (OI) at days 3 and 14
2. Physiological indices of acute lung injury, as measured by respiratory compliance (Cr_s), 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.

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 [PaO₂]/fraction of inspired oxygen [FiO₂] 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.

Previous inclusion criteria:

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 [PaO₂]/fraction of inspired oxygen [FiO₂] 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 48 hours of ALI onset.

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

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

Previous exclusion criteria:

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. 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**

United Kingdom

Northern Ireland

Study participating centre

Royal Victoria Hospital

Belfast

United Kingdom

BT12 6BN

Sponsor information

Organisation

Belfast Health and Social Care Trust (UK)

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

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	01/06/2017		Yes	No
Protocol article	protocol	18/02/2013		Yes	No

