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

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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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 (mean airway pressure [cm H20] x FiO2 x 100) = PaO2 (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 (Crs), 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 [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

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

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
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
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2nd Floor King Edward Building
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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?
Protocol article	protocol	18/02/2013		Yes	No
Results article	results	01/06/2017		Yes	No
HRA research summary			28/06/2023	No	No