

Activated protein C versus placebo in the treatment of INFlammatory or infectious Acute Lung Injury/acute respiratory distress syndrome (INFALI): a pathophysiological study on pulmonary microvascular permeability, apoptosis, inflammation and coagulation

Submission date 22/11/2006	Recruitment status No longer recruiting	☐ Prospectively registered ☐ Protocol
Registration date 22/11/2006	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 19/03/2014	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

Protocol serial number

Study information

Scientific Title

Acronym

INFALI

Study objectives

We hypothesise that systemic activated Protein C (aPC) will benefit patients with Acute Lung Injury (ALI)/ Acute Respiratory Distress Syndrome (ARDS), as caused by inflammatory as well as infectious disorders, in terms of gas exchange, edema and capillary leak in these lungs, as well as in ventilator-days (duration of mechanical ventilation) or change in ventilatory mode.

Please note that as of 24/06/2008 more details on the sources of funding have been added to this record (i.e., funding now confirmed). This can be seen below in the sources of funding section.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics approval received from the local medical ethics committee

Primary study design

Interventional

Study design

Randomised, multicentre, single-blinded, placebo controlled, parallel group trial

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Acute lung injury, acute respiratory distress syndrome

Interventions

After stratification patients will be randomly assigned to the aPC (24 mcg/kg/hr during [in total] 96 hours) or placebo group.

1. On day one and five a 67-Ga pulmonary leak index and a computed tomography (CT)-thorax will be performed
2. In mechanically ventilated patients: mini-broncho alveolar lavage (mini-BAL) every second day
3. Day one to five, seven, nine, 11, 13, 15 blood samples and a chest X-ray

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

Activated Protein C (aPC)

Primary outcome(s)

67-Gallium Pulmonary Leak Index (PLI).

Key secondary outcome(s)

1. Lung injury score
2. Inflammatory mediators/biomarkers (blood, mini-BAL)
3. Coagulation and fibrinolysis markers (blood, mini-BAL)
4. Apoptosis markers (blood, mini-BAL)
5. Mortality
6. Extra-vascular lung water
7. Gas exchange (compliance, partial pressure of oxygen in arterial blood [PaO₂]/fraction of inspired oxygen [FiO₂])
8. Radiographic abnormalities (X-ray, CT)
9. Change of ventilatory mode (non-invasive versus invasive)
10. Duration of mechanical ventilation

Completion date

01/09/2008

Eligibility

Key inclusion criteria

1. Age 18 to 75 years
2. Weight less than 135 kg
3. Recent onset (less than 24 hours) of ALI/ARDS, according to the American/European consensus criteria
4. ALI/ARDS due to severe sepsis reflecting single organ failure

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

Not Specified

Key exclusion criteria

1. Acute Physiology And Chronic Health Evaluation (APACHE II) score: 25 and more
2. Two or more failing organs
3. Thrombocyte count less than $30 \times 10^9/l$
4. Any major surgery within 12 hours before inclusion
5. Trauma patients at increased risk of bleeding
6. Acute bleeding
7. A history of severe head trauma that required hospitalisation, intracranial surgery, or stroke within three months of study entry
8. Known intracranial abnormality such as aneurysms, tumor, arterio-venous malformation
9. Known hypercoagulability:
 - 9.1. Resistance to protein C
 - 9.2. Hereditary deficiency of protein C, protein S, or anti-thrombin
 - 9.3. Presence of anticardiolipin antibody, antiphospholipid antibody, lupus anticoagulant or homocystinaemia
 - 9.4. Recently documented (within three months of study entry) or highly suspected deep vein thrombosis or pulmonary embolism
10. A history of congenital bleeding diathesis
11. Expected life expectancy less than 28 days (moribund state)
12. Preterminal illness
13. Pregnancy or breast feeding
14. Known portal hypertension with liver cirrhosis, oesophageal varices or both
15. Epidural catheter
16. Body weight more than 135 kg
17. Chronic renal insufficiency
18. Participation in another clinical trial
19. Patients with immune system impairment:
 - 19.1. Human immunodeficiency virus (HIV)-infected patients (CD4+ less than 50/ml)
 - 19.2. After bone-marrow, lung, liver, pancreas or small-bowel transplantation and treated with immunosuppressive therapy

Date of first enrolment

01/09/2006

Date of final enrolment

01/09/2008

Locations

Countries of recruitment

Netherlands

Study participating centre

VU Medical Center

Amsterdam

Netherlands

1007 MB

Sponsor information

Organisation

Vrije University Medical Center (VUMC) (The Netherlands)

ROR

<https://ror.org/00q6h8f30>

Funder(s)

Funder type

Industry

Funder Name

Added as of 24/06/2008:

Funder Name

Lilly Nederland B.V. (The Netherlands)

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	14/03/2014		Yes	No