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A pilot, double-blind, randomised, placebo-controlled, exploratory study to investigate the safety and effect of calf intestinal Alkaline Phosphatase in patients with SEPsis

Submission date 20/12/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 20/12/2005	**Overall study status** Completed	
Last Edited 06/07/2009	**Condition category** Infections and Infestations	

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

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NTR;137; CIAP 02-01

Study information

Scientific Title

Acronym
APSEP study

Study objectives
Unlike other potential sepsis treatments, alkaline phosphatase has been shown to act at the front end of the inflammatory cascade. By doing so, it eliminates the root cause of the Systemic Inflammatory Response Syndrome (SIRS), and prevents the progression into sepsis and septic shock.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the local medical ethics committee

Study design
Multicentre, randomised, double blind, placebo controlled, parallel group

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

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

Interventions
Patients will be assigned to receive either CIAP or placebo administered intravenously over 24 hours.

Patients randomised to CIAP will receive an initial bolus injection of 67.5 U/kg body weight administered over 10 minutes, followed by continuous infusion of 132.5 U/kg, administered over the remaining 23 hours and 50 minutes.

Patients randomised to placebo will receive the same quantities of corresponding injection fluids, without the active compound.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Calf Intestinal Alkaline Phosphatase (CIAP)

Primary outcome measure
Safety:
1. (Serious) adverse events
2. Antibodies against CIAP
3. Electrocardiogram (ECG) parameters
4. Biochemical safety parameters
5. Haematological parameters
6. Coagulation parameters

Efficacy (primary effect parameters):
1. C-Reactive Protein (CRP)
2. Plasma lactate
3. Cytokines (Tumour Necrotising Factor alpha [TNF-α], Interleukin-1 [IL-1], Interleukin-4 [IL-4], Interleukin-6 [IL-6], Interleukin-8 [IL-8] and Interleukin-10 [IL-10])
4. White cell differential cell count
5. Procalcitonin
6. Lipopolysaccharide (LPS)

Secondary outcome measures
Efficacy (secondary effect parameters):
1. Body temperature
2. Heart rate
3. Blood pressure
4. Acute Physiology And Chronic Health Evaluation (APACHE-II) score
5. Overall mortality at 28 days
6. Length of stay at Intensive Care Unit (ICU)
7. Number of days requiring mechanical ventilation
8. Length of stay in hospital
9. Sequential Organ Failure Assessment (SOFA)
10. Number of dysfunctional organs

Overall study start date
01/08/2004

Completion date
01/03/2006

Eligibility

Key inclusion criteria

1. Patients greater than or equal to 18 years and less than or equal to 80 years
2. Proven or suspected infection
3. Two out of four SIRS criteria of systemic inflammation, existing for less than 24 hours after admission in the intensive care unit:
a. core temperature greater than or equal to 38 or less than or equal to 36°Celsius
b. heart rate greater than of equal to 90 beats/min (unless the patient has a medical condition known to increase heart rate or is receiving treatment that would prevent tachycardia)
c. respiratory rate greater than or equal to 20 breaths/min, an arterial carbon dioxide pressure (PaCO2) less than or equal to 32 mmHg or the use of mechanical ventilation for an acute respiratory process
d. white-cell count greater than or equal to 12,000/mm^3 or less than or equal to 4,000/mm^3 or a differential count showing more than 10% immature neutrophils
4. Acute onset of end-organ dysfunction in the preceding 12 hours unrelated to the primary septic focus and not explained by any underlying chronic disease as indicated by one or more of the following:
a. sustained hypotension or organ dysfunction that is the result of sepsis and not the patients underlying disease or treatment, as evidenced by one or more of the following criteria for less than 12 hours:
i. systolic blood pressure less than or equal to 90 mmHg or mean arterial pressure less than or equal to 70 mmHg for at least one hour (by two or more measurements) despite adequate fluid intake, or
ii. a requirement for vasopressor support to maintain Mean Arterial Pressure (MAP)
b. acute renal failure, defined by either oliguria (a urine output less than or equal to 0.5 ml/kg /hour for at least two consecutive hours or a rise in serum creatinine concentration greater than or equal to 177 µmol/l (2.0 mg/dl) within the previous 48 hours, in the absence of primary underlying renal disease
c. acute alteration in mental state not due to sedation or of primary underlying disease of the central nervous system
d. acute hypoxemic respiratory failure, defined by a Partial Pressure of Oxygen in Arterial Blood (PaO2)/Fraction of Inspired Oxygen (FiO2) ratio less than 40 kPa (300 mmHg) in the absence of primary underlying pulmonary disease
e. disseminated intravascular coagulopathy defined by either:
i. platelet count less than or equal to 100 x 10^9/l
ii. coagulation abnormality (Prothrombin Time [PT] 1.2 times control or Activated Partial Thromboplastin Time [APTT] 1.2 times control)
f. metabolic acidosis defined as pH less than or equal to 7.30 or base excess less than or equal to -5 mmol/l in association with a plasma lactate more than or equal to 3.0 mmol/l
g. acute hepatic failure, defined by at least two of the following criteria, in absence of primary underlying hepatic disease:
i. serum bilirubin concentration more than 43 µmol/l (2.5 mg/dl)
ii. serum Alanine Aminotransferase (ALAT)/Aspartate Aminotransferase (ASAT) concentration more than twice the upper limit of normal range
iii. PT more than 1.5 times the control value or an International Normalised Ratio (INR) more than 1.5 in the absence of systemic anticoagulation
5. Written informed consent obtained

Participant type(s)
Patient

Age group

Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
32

Key exclusion criteria
1. Pregnant or lactating women
2. Known Human Immunodeficiency Virus (HIV) seropositive patients
3. Patients receiving immunosuppressive therapy or high doses of glucocorticosteroids (defined as more than 1 mg/kg/day) equivalent to prednisone 1 mg/kg/day
4. Patients expected to have rapidly fatal disease within 24 hours
5. Known confirmed gram-positive sepsis
6. Known confirmed fungal sepsis
7. Chronic renal failure requiring haemodialysis or peritoneal dialysis
8. Acute pancreatitis with no established source of infection
9. Patients not expected to survive for 28 days due to other medical conditions such as end-stage neoplasm or other diseases
10. Participation in another investigational study within 90 days prior to start of the study which might interfere with this study
11. Previous administration of CIAP
12. Known allergy for cow milk

Date of first enrolment
01/08/2004

Date of final enrolment
01/03/2006

Locations

Countries of recruitment
Netherlands

Study participating centre
Rumpsterweg 6
Bunnik
Netherlands
3981 AK

Sponsor information

Organisation
AM-Pharma B.V. (Netherlands)

Sponsor details
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Sponsor type
Industry

Website
http://www.am-pharma.com/

ROR
https://ror.org/02bpbnv34

Funder(s)

Funder type
Industry

Funder Name
AM-Pharma B.V. (Netherlands)

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?
Results article	results	01/02/2009		Yes	No