A pilot, double-blind, randomised, placebo-controlled, exploratory study to investigate the safety and effect of Calf Intestinal Alkaline Phosphatase in patients with sepsis.

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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 SIRS, and prevents the progression into sepsis and septic shock.

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON19934

Bron
NTR

Verkorte titel
APSEP study

Aandoening

Sepsis.

Ondersteuning

Primaire sponsor: AM-Pharma B.V.
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THE NETHERLANDS
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Overige ondersteuning: N/A

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Criteria for evaluation of safety:
1. (Serious) adverse events;

2. Antibodies against CIAP;

3. ECG parameters;

4. Biochemical safety parameters;

5. Hematological parameters;

6. Coagulation parameters.

Efficacy: (primary effect parameters):

7. CRP;

8. Plasma lactate;

9. Cytokines (TNF-, IL-1, IL-4, IL-6, IL-8 IL-10);

10. White cell differential cell count;

11. Procalcitonin;

12. LPS.

Toelichting onderzoek

Achtergrond van het onderzoek

Objectives:

for this trial are to investigate CIAP in sepsis patients assessing the safety and tolerability, the pharmaco kinetics of CIAP, and the effect of CIAP on inflammation parameters and on clinical parameters.

Eligible patients will receive either CIAP or matching placebo in a double blind, randomized design and following a 2:1 ratio.
All medication will be given in addition to standard care for sepsis patients. Patients will be followed for 28 days after the start of study medication administration.

Doel van het onderzoek

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 SIRS,

and prevents the progression into sepsis and septic shock.

Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

Patients will be assigned to receive either CIAP or placebo administered intravenously over 24 hours.
Patients randomized 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 randomized to placebo will receive the same quantities of corresponding injection fluids, without the active compound.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Patients >= 18 years and <= 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 >= 38 or <= 36 Celsius;

b. Heart rate >= 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 >= 20 breaths/min, a PaCO2 <= 32 mmHg or the use of mechanical ventilation for an acute respiratory process;

d. White-cell count >= 12.000/mm3 or <= 4.000/mm3 or a differential count showing > 10 percent 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 ≥ 1 (one or more) of the following:

4.1 Sustained hypotension or organ dysfunction that is the result of sepsis and not the patient’s underlying disease or treatment, as evidenced by one or more of the following criteria for less than 12 hours:

4.1.a Systolic blood pressure <= 90 mmHg or mean arterial pressure <= 70 mmHg for at least one hour (by two or more measurements) despite adequate fluid intake, or

4.1.b A requirement for vasopressor support to maintain MAP

4.2 Acute renal failure, defined by either oliguria (a urine output <= 0.5 ml/kg/hr for at least 2 consecutive hours or a rise in serum creatinine concentration >= 177 µmol/l (2.0 mg/dl) within the previous 48 hours, in the absence of primary underlying renal disease.

4.3 Acute alteration in mental state not due to sedation or of primary underlying disease of the central nervous system.

4.4 Acute hypoxemic respiratory failure, defined by a PaO2(/FiO2 ratio <40 kPa (300 mmHg) in the absence of primary underlying pulmonary disease.

4.5 Disseminated intravascular coagulopathy defined by either:

4.5.a Platelet count <= 100 * 109/L

4.5.b Coagulation abnormality (PT 1,2 times control or APTT 1,2 times control)

4.6 Metabolic acidosis defined as pH <= 7.30 or base excess >= -5 mmol/L in association with a plasma lactate >= 3.0 mmol/L

4.7 Acute hepatic failure, defined by at least 2 of the following criteria, in absence of primary underlying hepatic disease:

4.7.a Serum bilirubin concentration > 43 µmol/l (2.5 mg/dl)

4.7.b Serum ALAT/ASAT concentration > twice the upper limit of normal range

4.7.c Prothrombin time > 1.5 times the control value or an International Normalized Ratio > 1.5 in the absence of systemic anticoagulation

5. Written informed consent obtained.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Pregnant or lactating women;

2. Known HIV seropositive patients;

3. Patients receiving immunosuppressive therapy or high doses of glucocortico steroids (defined as > 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 hemodialysis 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 cowmilk.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-08-2004
Aantal proefpersonen:	32
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	24-08-2005
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL106
NTR-old	NTR137
Ander register	: CIAP 02-01
ISRCTN	ISRCTN49482187

Resultaten

Samenvatting resultaten
N/A