A Phase-II, double-blind, randomized, placebo-controlled study on the safety and early efficacy of Alkaline Phosphatase in sepsis patients with Renal Failure.

Published: 19-09-2007
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To establish the safety and and tolerability and early efficacy of Alkaline phosphatase in the treatment of sepsis patients with renal failure.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON33810

Source
ToetsingOnline

Brief title
niet van toepassing

Condition

- Bacterial infectious disorders
- Nephropathies

Synonym
Acute renal failure in sepsis (Bloodpoisoning) patients

Research involving
Human

Sponsors and support

Primary sponsor: AM-Pharma B.V.
Source(s) of monetary or material Support: AM-Pharma B.V.

Intervention

Keyword: Alkaline Phosphatase, Efficacy, Renal Failure, Safety

Outcome measures

Primary outcome

To investigate the safety and tolerability of AP in sepsis patients with renal failure

To investigate the pharmacokinetics of AP in sepsis patients with renal failure

To investigate the effect of AP on inflammatory parameters in sepsis patients with renal failure

To investigate the effect of AP on renal failure and associated clinical parameters in sepsis patients with renal failure

Secondary outcome

Not applicable

Study description

Background summary

A previous clinical study conducted in centers in The Netherlands and Belgium have shown a substantial clinical benefit of AP treatment in patients with sepsis and associated acute renal failure (see Introduction above). The latter

results require confirmation in a prospective study, as the current subject of this Protocol.

Study objective

To establish the safety and and tolerability and early efficacy of Alkaline phosphatase in the treatment of sepsis patients with renal failure.

Study design

Eligible patients will receive AP or matching placebo in a double-blind, randomized design and following a 1:1 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.

Intervention

Patients randomized to CIAP will receive an initial bolus injection of 67.5 U/kg body weight administered over 10 minutes, followed by a continuous infusion of 132.5U/Kg/24 hours administered over the remaining 48 hours.
Patients will be followed for 28 days after the start of study medication.

Study burden and risks

Extra blood will be drawn (150mL over a period of 28 days)

Contacts

Public
Selecteer

Rumpsterweg 6
3981 AK Bunnik
Nederland
Scientific
Selecteer

Rumpsterweg 6
3981 AK Bunnik
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Patients >=18 years and <=80 years.
• Proven or suspected infection.
• Two out of four SIRS criteria of systemic inflammation, as follows:
• Core temperature >=38°Celsius or <=36° Celsius.
• 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).
• Respiratory rate >=20 breaths/min, a PaCO2 <=32mmHg or the use of mechanical ventilation for an acute respiratory process.
• White-cell count >=12,000/mm3 or <=4,000/mm3 or a differential count showing >10 percent immature neutrophils.
• Acute renal failure, defined as - a rise in serum creatinine level to >= 150µmol/l within the previous 48 hours, in the absence of primary underlying renal disease OR - minimally a stage 1 Kidney injury according to AKIN creatinine criteria: Increase in serum creatinine >= 26.2 umol/l (0.3mg/dl) or increase to >= 150% (>=1.5 fold) from baseline in the previous 48 hours (in the abscence of primary underlying renal disease and where baseline creatinine is less than 150umol/l) OR -minimally a stage 1 Kidney Injury according to AKIN Urine utput criteria: oliguria, defined as urine output <=0.5mL/kg/hr for >=6 hours and following adequate fluid resuscitation when applicable, in the absence of primary underlying renal disease and where baseline creatinine is less than 150 umol/l,
• patient already on renal replacement therapy (RRT, dialysis) due to renal impairment secondary to sepsis.
• Written informed consent obtained prior to any study intervention.
In addition to the above, the following common conditions may be present (not compulsory for patient qualification for enrolment):
• Acute onset of end-organ dysfunction (other than renal failure) in the preceding 12 hours unrelated to the primary septic focus and not explained by any underlying chronic disease such as:
• 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:
• Systolic blood pressure <=90mmHg or mean arterial pressure <=70mmHg for at least one hour (by two or more measurements) despite adequate fluid intake, OR
• requirement for vasopressor support to maintain MAP
• Acute alteration in mental state not due to sedation or of primary underlying disease of the central nervous system.
• Acute hypoxemic respiratory failure, defined by a PaO2(/FiO2 ratio <40kPa (300mmHg) in the absence of primary underlying pulmonary disease.
• Disseminated intravascular coagulopathy defined by either:
• Platelet count <=100*109/L
• Coagulation abnormality (PT=1.2 times control or APTT=1.2 times control)
• Metabolic acidosis defined as pH*7.30 or base excess *-5mmol/L in association with a plasma lactate *3.0mmol/L
• Acute hepatic failure, defined by at least 2 of the following criteria, in absence of primary underlying hepatic disease:
• serum bilirubin concentration >43µmol/L
• serum ALAT/ASAT concentration greater than twice the upper limit of normal range
• prothrombin time >1.5 times the control value OR an International Normalized Ratio >1.5 in the absence

Exclusion criteria

• Pregnant women or nursing mothers and fecund females who are not on effective contraception (chemical: pill; or mechanical: IUD)
• Known HIV (sero-positive) patients
• Patients already on dialysis (RRT) at entry
• Patients receiving immunosuppressant therapy or on chronic high doses of steroids equivalent to prednisone 1mg/Kg/day
• Patients expected to have rapidly fatal disease within 24 hours
• Known confirmed gram-positive sepsis
• Known confirmed fungal sepsis
• Acute pancreatitis with no established source of infection
• Patients not expected to survive for 28 days due to other medical conditions such as end-stage neoplasm or other diseases
• Participation in another investigational study within 90 days prior to start of the study which might interfere with this study
• Any previous administration of active study medication.
• Known allergy for dairy (bovine) products including cow milk.
• Sepsis without renal failure as defined in the Entry Criteria.
• History of chronic renal failure or history of persistent creatinine level equal or greater than 150umol/L prior to entry for reasons other than the current sepsis condition.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-05-2008
Enrollment:	39
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	not applicable
Generic name:	Alkaline Phosphatase

Ethics review

Approved WMO Date:	19-09-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-02-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	13-06-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-09-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-01-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-02-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-03-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-05-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-05-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-05-2009

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-06-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-07-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-08-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2007-003866-16-NL
ClinicalTrials.gov	NCT00511186
CCMO	NL18811.000.07