Efficacy and Safety of Drotrecogin Alfa (Activated) in Adult Patients with Septic Shock

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To demonstrate that treatment with drotrecogin alfa (activated) 24 mcg/kg/h administered as an intravenous infusion for 96 hours reduces 28 day all-cause mortality in adult patients with septic shock compared with placebo.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	General system disorders NEC
Study type	Interventional

Summary

ID

NL-OMON31460

Source
ToetsingOnline

Brief title
PROWESS-SHOCK

Condition

- General system disorders NEC

Synonym
Lack of circulating volume due to bacterial infection of the blood

Research involving
Human

Sponsors and support

Primary sponsor: Eli Lilly
Source(s) of monetary or material Support: Eli Lilly

Intervention

Keyword: 28-day mortality, Drotrecogin Alfa (activated), Placebo-controlled, Septic Shock

Outcome measures

Primary outcome

All-cause mortalilty after 28 days

Secondary outcome

1. Death related to severe sepsis, that is, related to severe sepsis or a sequela of sepsis based on the interpretation of the investigator.

2. Cardiovascular events: the need for vasoactive drugs or hypotension.

3. Respiratory events: decreased PaO2/FiO2, mechanical ventilation, hypoxia, acute respiratory distress syndrome, acute lung injury, or respiratory failure.

4. Hepatic events: hepatic injury or liver dysfunction that leads to an increase from baseline in the serum level of bilirubin.

5. Renal events: renal failure, renal insufficiency, or renal injury that leads to an increase from baseline in serum creatinine.

6. Hematologic/coagulation events: coagulopathy, disseminated intravascular coagulation, thrombocytopenia, or thrombocytosis.

7. Systemic inflammatory response syndrome related criteria: tachypnea, hypopnea, leukocytosis, leukopenia, hypothermia, hyperthermia, tachycardia, or bradycardia.

Study description

Background summary

Page 15 and 16 of the study protocol:
Septic shock as an independent criterion for the use of drotregocin alfa (activated) has not been studied in previous trials. Drotregocin alfa (activated) received approval on the basis of a study in patients with severe shock (PROWESS). Since registration, two placebo-controlled studies of drotegocin alfa (activated) have not shown evidence of efficacy. The EMEA have requested the sponsor, Eli Lilly,an additional placebo-controlled study to further evaluate the efficacy and safety of drotrecogin alfa (activated) and to better identify patients who would benefit from drotrecogin alfa (activated) treatment.

Study objective

To demonstrate that treatment with drotrecogin alfa (activated) 24 mcg/kg/h administered as an intravenous infusion for 96 hours reduces 28 day all-cause mortality in adult patients with septic shock compared with placebo.

Study design

A multicenter, randomized, double-blind, parallel, placebo controlled, Phase 3 study of drotrecogin alfa (activated) in patients with septic shock. Planned enrollment in the study is approximately 1500 patients. Patients will be randomly assigned to either the drotrecogin alfa (activated) or placebo treatment group in a 1:1 ratio. Randomization will be stratified by investigative site. The study consists of 4 treatment periods: pretreatment, treatment, post treatment, and follow-up

Intervention

Subjects will be randomly assigned to either drotrecogin alfa (activated) 24 mcg/kg/h administered as an intravenous infusion for 96 hours or to placebo.

Study burden and risks

In order to enroll eligible patients and to monitor their safety, the Vandebilt coordinating centre (VCC) is contracted to support the investigative sites. The VCC will be consulted by the study team at the sites to confirm eligibility of each patient for inclusion in the study. The VCC will also be notified by the sites of all SAEs. This will need to be done within 24 hours that the investigator was aware of the SAE. VCC will process all initial SAEs per protocol criteria on forms provided by Parexel.

The patient is at no greater risk than with the standard treatment he/she would receive

Pharmaco-genetic substudy: Participation is voluntary and is not a prerequisite

for participation in the study. In total, four bloodsamples (two before the start of the study drug infusion, one sample on day one and one sample on day four after starting the study drug infusion) will be taken from those patients who have signed the separate pharmaco-genetic patient information form.

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patient must be an adult (18 years or older)
2. Patient must have evidence of an infection for which the patient is receiving intravenous antimicrobial therapy
3. Patient must have systemic inflammatory response syndrome (SIRS).
4. Patient must have septic shock
5. Patients must remain vasopressor dependent throughout the pretreatment period and

through the time of randomization

Exclusion criteria

Patients who, prior to the start of study drug, have received vasopressor therapy (at any dose) for greater than 24 hours or have sepsis-induced organ dysfunction for greater than 36 hours, patients who have had surgery performed within the 12-hour period immediately preceding the study drug infusion, have an active internal bleeding or are at increased risk for bleeding, patients who are not expected to survive 28 days given their preexisting uncorrectable medical condition or are receiving concommitant therapies that will have an impact on their wellbeing

Study design

Design

Study phase:	3
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):	23-05-2009
Enrollment:	100
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Xigris
Generic name:	Drotrecogin Alfa (activated)

Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	28-12-2007
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-12-2008
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-06-2009
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2007-005441-38-NL
CCMO	NL21012.091.07