A randomised, double-blind, parallel-group, placebo-controlled phase III study to evaluate the efficacy and safety of desmoteplase in subjects with acute ischemic stroke.

Published: 29-09-2008
Last updated: 06-05-2024

The primary objective of the study is to evaluate the efficacy of desmoteplase 90µg/kg versus placebo in terms of favourable outcome at Day 90 in subjects with acute ischemic stroke. Secondary objectives are to evaluate: the efficacy of desmoteplase...

Ethical review	Approved WMO
Status	Pending
Health condition type	Central nervous system vascular disorders
Study type	Interventional

Summary

ID

NL-OMON32542

Source
ToetsingOnline

Brief title
DIAS-3

Condition

- Central nervous system vascular disorders

Synonym
ischemic stroke

Research involving
Human

Sponsors and support

Primary sponsor: Lundbeck
Source(s) of monetary or material Support: H. Lundbeck A/S

Intervention

Keyword: acute ischemic stroke, desmoteplase, DIAS-3

Outcome measures

Primary outcome

Modified Rankin Scale (mRS) score at Day 90

Secondary outcome

National Institutes of Health Stroke Scale (NIHSS)

Recanalistion at 12-24 hours (sub-study)

Study description

Background summary

Acute ischemic stroke is a major cause of mortality and of long-term disability. Thrombolysis targets the clots that occlude brain vessels in acute ischemic stroke and therefore has the potential to provide significant improvement of clinical outcome. The only thrombolytic intervention currently approved for acute ischemic stroke needs to be administered within 3 hours after symptom occurrence, and has a significant risk inducing intracerebral haemorrhage. Desmoteplase has properties that indicate potential for a better clinical efficacy and a lower risk of bleeding that may allow extension of the time window for treatment to 9 hours after symptom onset.

Study objective

The primary objective of the study is to evaluate the efficacy of desmoteplase 90µg/kg versus placebo in terms of favourable outcome at Day 90 in subjects with acute ischemic stroke. Secondary objectives are to evaluate: the efficacy of desmoteplase 90µg/kg versus placebo in terms of favourable outcome at Day 7/Discharge and Day 30 in subjects with acute ischemic stroke, the efficacy of

desmoteplase 90µg/kg versus placebo in terms of favourable outcome at Day 90 in the subgroup of patients with a baseline core-lesion volume < 25 cc, recanalisation associated with 90µg/kg versus placebo in the subgroup of patients with follow-up angiography at 12-24 hours, safety and tolerability of desmoteplase, incidence of symptomatic intracranial haemorrhage (sICH), mortality in the treatment groups, immunogenicity of desmoteplase, pharmacokinetics/pharmacodynamics of desmoteplase, impact of treatment on subject's quality of life, impact of treatment on utilization of resources.

Study design

The study will be conducted as a prospective, randomised, double-blind, placebo-controlled, multinational, multi-centre, parallel-group study.
Study duration per subject will be 90 days from the time of the Investigational Medicinal Product (IMP) administration.
The study will investigate one dose of desmoteplase (90µg/kg) versus placebo given as a single intravenous bolus.
A diagnostic neuroimaging screening with MRI or CT will be used to identify eligible subjects with occlusion or high grade stenosis in proximal cerebral arteries and with no signs of extensive infarction, intracranial haemorrhage or subacute infarctions. After eligibility and baseline assessments, subjects will receive treatment with the IMP within 3-9 hours after the onset of stroke symptoms. In the subsequent hours and days patients will undergo regular safety and efficacy assessments until they are discharged. Study procedures/examinations will be performed between 0.5 and 9 hours, between 12 and 24 hours after IM administration, at Day 7 or discharge (if earlier), at Day 30 and at Day 90.
An imaging scan 12-24 hours after IMP administration will be used to mintor subjects for intracranial bleedings, to assess infarct size, and in subjects ondergoing a folow-up angiogram (optional), to assess recanalisation.

Intervention

90µg/kg desmoteplase, or placebo, administered as a single intravenous bolus injection during 1-2 minutes.

Study burden and risks

At baseline a physical and neurological examination will be performed. Blood pressure, pulse rate and weight will be assessed. An ECG will be recorded, and blood samples will be taken for safety laboratory tests. A diagnostic MRI or perfusion CT scan will be conducted. In case of eligibility study medication will be administered as a single IV bolus injection during 1-2 minutes. As follow-up over a 90 day period (7 assessments/visits), blood sampling will take place 6 times, vital signs will be assessed 7 times, one ECG wil be recorded, one MRI/CT scan will be conducted, and various rating scales will be assessed

2-5 times. At the final visit the physical/neurological examination will be repeated.
Major risk of thrombolysis is the occurrence of intracerebral haemorrhage, which occurred in 3.5% of the patients treated with desmoteplase 90µg/kg in previous clinical studies (refer to IB).
Benefit of participation is a potential clinical improvement in a patient group, suffering from a life threatening and disabling disorder, who currently have insufficient adequate treatment modalities available.

Contacts

Public
Lundbeck

Postbus 12021
1100 AA Amsterdam
NL
Scientific
Lundbeck

Postbus 12021
1100 AA Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Clinical diagnosis of acute ischemic stroke
• Male or female between 18 and 85 years of age inclusive.

• Treatment of the subject can be initiated within 3-9 hours after the onset of stroke symptoms.
• The subject has a score of 4-24 inclusive on the NIHSS with clinical signs of hemispheric infarction (for example, hemiparesis)
• The subject shows occlusion or high-grade stenosis as assessed by MRA or CTA in proximal cerebral arteries that correspond to the acute clinical deficit.
• The subject should receive IMP within 60 minutes after completion of diagnostic imaging screening

Exclusion criteria

• The subject has a pre-stroke mRS > 1 indicating previously disability
• The subject has previously been exposed to desmoteplase
• The subject shows signs of extensive early infarction on MRI or CT in any affected area
• The subject has imaging evidence of ICH or SAH (regardless of age of the bleeding)
• The subject has an internal carotid artery occlusion on the side of the stroke lesion
• The subject has been treated with heparin in the past 48 hours and has a prolonged partial thromboplastin time exceeding the upper limit of the local laboratory normal range.
• The subject is on oral anticoagulants and has a prolonged prothrombin time (INR > 1.6)
• The subject has been treated with glycoprotein IIb - IIIa inhibitors within the past 72 hours.
• The subject has been treated with factor Xa inhibitors in the past 72 hours
• The subject has been treated with a thrombolytic agent within the past 72 hours

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: Pending

Start date (anticipated):	01-12-2008
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	desmoteplase

Ethics review

Approved WMO Date:	29-09-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-02-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-12-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-04-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-06-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2008-000622-40-NL
CCMO	NL24948.042.08