A Phase IIa, multi-centre, randomised, double-blind, placebo controlled, clinical study investigating the safety, tolerability and pharmacokinetics of two different infusion doses over 72 hours of a new regimen and new formulation of MCI-186 in subjects with acute ischemic stroke

Published: 16-10-2008
Last updated: 06-05-2024

STUDY OBJECTIVESPrimary objectiveTo assess the safety, tolerability and local tolerance of two different intravenous infusion doses over 72 hours of a new dosing regimen and a new formulation of MCI-186 in subjects with acute ischemic stroke....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Decreased and nonspecific blood pressure disorders and shock
Study type	Interventional

Summary

ID

NL-OMON35656

Source
ToetsingOnline

Brief title
MCI-186-E04

Condition

- Decreased and nonspecific blood pressure disorders and shock

Synonym
Acute Ischemic Stroke (AIS) - stroke

Research involving
Human

Sponsors and support

Primary sponsor: Mitsubishi Pharma Corporation
Source(s) of monetary or material Support: Mitsubishi Tanabe Pharma Corporation

Intervention

Keyword: - acute ischemic stroke, - Edaravone, - MCI-186

Outcome measures

Primary outcome

Primary Endpoint

Adverse Events (safety and tolerability)

Secondary outcome

Secondary Endpoints

1) Concentrations of MCI-186 to assess steady state

2) Changes on clinical and neurological measurements

• Changes on scores of mRS, NIHSS, Barthel Index and GOS

• CT scan: changes on extension of lesion, severity of edema, presence or

absence of mass effect and intracranial hemorrhage.

Study description

Background summary

MCI-186 is a novel free radical scavenging drug that exerts its neuroprotective activity by inhibiting the lipid peroxidazation of phospholipid membranes caused by free radicals that occur in the brain in subjects with acute ischemic stroke (AIS).

Mitsubishi Tanabe Pharma Corporation developed MCI-186 for the indication of AIS in a series of clinical trials in Japan, where it was granted marketing approval in 2001. The approved dosing regime in Japan is 30 mg/body/30 min b.i.d. for 14 days.

For the last years Mitsubishi Tanabe Pharma has being working on the design of the clinical program development of MCI-186 in Europe with European and USA AIS experts.

Based on knowledge accumulated during the last decade on AIS and clinical development of neuroprotectants (e.g. STAIR consensus group (http://thestair.com/)) the experts consulted suggested a different regimen paradigm from the one actually being used with Edavarone in Japan.

Accepting the AIS experts suggestions Mitsubishi conducted two Phase I studies in Europe (E01 and E02 studies). Both studies had as objective to evaluate a new formulation and possible dosing to support a new regimen paradigm.

Encouraged by the results from both phase I studies the objective of this study is to start the clinical program with subjects using the new paradigm regimen proposed by the AIS experts.

Study objective

STUDY OBJECTIVES

Primary objective

To assess the safety, tolerability and local tolerance of two different intravenous infusion doses over 72 hours of a new dosing regimen and a new formulation of MCI-186 in subjects with acute ischemic stroke.
Secondary objectives

1) To investigate the steady state plasma levels and terminal elimination half life of two different intravenous infusion doses over 72 hours of a new dose regimen and a new formulation of MCI-186 in subjects with acute ischemic stroke

2) To review the routine clinical and neurological assessments data of AIS over a period of 87 days from the start of the intravenous infusion.

Study design

This study is a Phase IIa, multi-centre, randomised, double-blind, placebo controlled, clinical study investigating the safety, tolerability and pharmacokinetics of two different infusion doses over 72 hours of a new regimen and new formulation of MCI-186 in subjects with acute ischemic stroke.

(* On page 2 of the Protocol a 'Summary study design and population' has been pictures. The scheme could not be copied into this ABR Form).

There are two groups namely 1 and 2. PLEASE ASK YOUR RESEARCH DOCTOR IN WHICH GROUP YOU MAY BE ENROLLED.

The dosing on both groups will be based on individual patient weight.

Group 1 will receive a continuous intravenous infusion of MCI-186 over 72 hours, or a continuous infusion of placebo over 72 hours (Loading dose 0.08 mg/kg (3 min) + 0.2 mg/kg/h intravenous infusion over 72h).

When the results of the Group 1 are known

Group 2 will receive a continuous intravenous infusion of MCI-186 over 72 hours that is up to two times the strength used in Group 1, or an infusion of placebo over 72 hours (Loading dose 0.16 mg/kg (3 min) + 0.4 mg/kg/h intravenous infusion over 72h).

The dose for Group 2 will be decided depending on the results from Group 1.

The decision to change the dosage for Group 2 (or keep it at the dose level stated above) will be made after an independent panel of stroke experts carefully examined all results from Group 1. Your research doctor as well as the Ethics Committee will be informed of the independent panel decision before Group 2 can starts.

Intervention

- Venapunction
- Intraveneus injection
- CT scan

Study burden and risks

As with any treatment the subject may experience side effects. A common side

effect that has been reported is abnormal liver function. Uncommon side effects reported are low platelets, anaemia, rise in temperature, increase uric acid or decreased protein in the blood, rash, renal impairment and blood or protein in the urine.

Rare side effects that have been reported are a change in the blood clotting, changes in potassium in the blood, changes in the lungs, nausea, vomiting, hepatitis (liver inflammation), jaundice, itching, urticaria, erythema (red spots on the skin), nephrotic syndrome (a disorder in which the blood filtering by the kidneys is disturbed), injection site reactions and headache.

Very rare side effects reported are low white cells in the blood, anaphylactic shock (a life-threatening situation due to an allergic reaction in the body) and pains in the muscles. Subjects may experience slight discomfort or bruising in the arms from the blood sampling and infusion. In addition the subject may experience irritation of the vein into which the study drug is infused.

Contacts

Public
Mitsubishi Pharma Corporation

Dashwood House, 69 Old Broad Street
London, EC2M 1QS
GB
Scientific
Mitsubishi Pharma Corporation

Dashwood House, 69 Old Broad Street
London, EC2M 1QS
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion Criteria;Subjects must meet the following criteria in order to be deemed suitable for inclusion in the study:;1. Male or female, aged 40-80 years old;2. Full functional independence prior to the present stroke (as evidenced by a pre-morbid modified Rankin Scale score of 0-2);3. Clinical diagnosis of acute stroke with CT scan ruling out intracranial hemorrhage;4. Onset of symptoms within 1-24 hours of commencement of infusion of study drug;5. Measurable deficit on NIHSS (as evidenced by a score of 3-15)
(See protocol Amendment 2, dated 12 May 2009).;6. Full consciousness (i.e. the score for NIHSS item 1a=0);7. Written valid informed consent is obtained from the subject or his/her next of kin or legal representative if the subject is fully conscious (i.e. the score for NIHSS item 1a = 0) but unable to read and/or sign the ICF, in accordance with National legislation and local IRB requirements.

Exclusion criteria

Exclusion Criteria;If subjects meet any of the following criteria, they CANNOT be entered into the study:;1. Subjects who are unlikely to complete the infusion of investigational product and/or are unlikely to undergo active medical management during that period due to a severe clinical condition.;2. Subjects unlikely to survive the acute period of stroke.;3. Subjects with severe illness with life expectancy less than 6 months.;4. Body weight in excess of 120 kg.;5. Subjects who have received rTPA or other thrombolytics (e.g. urokinase, streptokinase, reteplase, tenecteplase) within the previous 24 hours.;6. Subjects who have infection under antibiotic treatment at the enrollment.;7. Likelihood of forbidden concomitant therapy such as vascular surgery, coronary artery bypass graft (CABG), valve replacement, or carotid endarterectomy (CEA).;8. Evidence of cerebral herniation.;9. Subjects with confounding neurological diseases such as dementia.;10. Subjects with CADASIL, Moya Moya, or carotid dissection.;11. Subjects who have experienced a stroke within the previous 3 months (Note: subjects who have recently experienced a TIA, but whose premorbid mRS prior to their stroke is 0-2, will be allowed to enter the study).;12. History of peripheral vascular disease.;13. Subjects with Diabetes Mellitus who have a history of peripheral neuropathy or significant evidence of peripheral neuropathy on routine neurological examination.;14. Known severe kidney disorder (or estimated creatinine clearance of <30 mL/min).;15. Known severe hepatic disorder, or elevated liver enzymes (at least 2 of ALT, AST, and gamma GT) greater than 3 times the upper limit of normal (>3 x ULN).;16. Evidence from admission imaging tests of infarction involving >1/3 of MCA territory, orentire ACA territory involvement, or internal carotid artery (ICA) occlusions without coexisting separate occlusion of the middle cerebral artery (because of the difficulty distinguishing between chronic and acute ICA lesions in such subjects).;17. Pathology other than cerebral infarction on any admission imaging tests (e.g. ICH or SAH, AV malformation, cerebral aneurysm, or cerebral

neoplasm);18. Current or previous known excessive alcohol use or dependence.;19. Current known illicit drug use or dependence.;20. Participation in a previous clinical study within 30 days.;21. Subjects unlikely to be able and willing to attend all study follow-up visits.;22. Any other conditions which in the opinion of the investigator deem the subject ineligible for inclusion.;23. Females who are pregnant or intend to become pregnant or subjects (male and female) who do not agree to use effective contraception for 3 months after end of treatment.

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:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-04-2009
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Niet van toepassing.
Generic name:	Niet van toepassing.

Ethics review

Approved WMO

Date:	16-10-2008

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-01-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-06-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-07-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-10-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-10-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-11-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-01-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2008-003397-17-NL
CCMO	NL25267.078.08