A randomized, double blind, placebo-controlled single ascending dose study on the safety, tolerability, pharmacokinetics and pharmacodynamics of ACT017 in healthy volunteers

Published: 04-10-2017
Last updated: 12-04-2024

PRIMARY OBJECTIVETo evaluate the safety and tolerability of single ascending, intravenous doses of ACT017 administered as a 6-hour intravenous (i.v.) infusionSECONDARY OBJECTIVES* To evaluate the pharmacokinetics of single ascending, intravenous...

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

Summary

ID

NL-OMON44567

Source
ToetsingOnline

Brief title
ACT-CS-001 (CS0278)

Condition

- Central nervous system vascular disorders

Synonym
cerebral infarction, stroke

Research involving

Human

Sponsors and support

Primary sponsor: Acticor Biotech SAS
Source(s) of monetary or material Support: Acticor Biotech SAS

Intervention

Keyword: pharmacodynamics, pharmacokinetics, safety, tolerability

Outcome measures

Primary outcome

Safety

* Adverse Events (AEs)

* Clinical laboratory results

* Electrocardiogram (ECG)

* Vital signs

* Coagulation parameters (PT, PTT, INR)

* Platelet count

* GPVI expression

* Immunogenicity / anti-drug antibodies (ADA)

Secondary outcome

Pharmacokinetics

Pharmacokinetic parameters will be derived by non-compartmental analysis of the platelet free plasma concentration-time profiles. Details will be specified in the pharmacokinetics (PK) analytical plan.

Pharmacodynamics

* Bleeding time

* Collagen-induced platelet aggregation

Study description

Background summary

Blood platelets are critically involved in cardiovascular diseases including stroke. This is why antiplatelet agents are in first line of therapy and secondary prevention in coronary artery diseases. The use of antiplatelet agents is also suitable to treat stroke and prevent recurrence but the currently available molecules are not recommended at the acute phase (0 to 12 hours) due to the associated risk of hemorrhagic transformation. Early administration of intravenous aspirin in patients with acute ischemic stroke treated with rtPA is associated with increased of intracranial hemorrhage. Therefore, there is still a need for a safe and efficient antithrombotic agent administrable at the acute phase without inducing a bleeding risk in order to reduce the size of the clot, to favor cerebral reperfusion and to prevent recurrences.

Study objective

PRIMARY OBJECTIVE
To evaluate the safety and tolerability of single ascending, intravenous doses of ACT017 administered as a 6-hour intravenous (i.v.) infusion

SECONDARY OBJECTIVES
* To evaluate the pharmacokinetics of single ascending, intravenous doses of ACT017 administered as a 6-hour i.v. infusion
* To evaluate the pharmacodynamics (i.e. inhibition of platelet aggregation and absence of an effect on bleeding time) of single ascending, intravenous doses of ACT017 administered as a 6-hour i.v. infusion

Study design

Single-center, Phase I, single ascending dose (SAD) study with a randomized, double-blind, placebo-controlled design in 6 treatment groups of 8 subjects (6 active; 2 placebo), in which treatments are given as a 6-hour i.v. infusion.

Intervention

Screening
This includes an evaluation of the inclusion and exclusion criteria to check for eligibility. This evaluation will be performed within 2 to 28 days before study drug administration.
In-clinic period
After a re-evaluation of the inclusion and exclusion criteria on Day -1, eligible subjects will enter the in-clinic phase and leave on the morning of Day 3 after all study related procedures and approval by the Investigator. On Day 1, the study drug will be given once as an infusion of 6 hours. During this in-clinic phase, documentation of AEs will be done, in combination with blood sampling for pharmacokinetics (PK), blood sampling for pharmacodynamics (PD), clinical laboratory tests, urine collection, physical examination, weight, vital signs, and ECG.
Follow-up
Follow-up will take place on Day 7 ±2 days. During this visit, documentation of AEs will be done, in combination with vital signs, physical examination (including weight), blood sampling for PD, clinical laboratory tests, and ECG.

Study burden and risks

The study drug ACT017 has not been administered to humans before. ACT has been administered to animals, as required by regulatory (health) authorities. The dose has been selected based on the results of animal testing. The health risks are limited at these dose levels. Disadvantages of participation in the study may be the possible discomforts of the measurements performed in the study and the possible occurrence of side effects.

The blood collection procedure is not dangerous, but may cause discomfort or bruising. Occasionally, fainting, bleeding or an infection at the blood sampling site can occur.

One of the methods evaluating the clot properties of your blood uses a device making a small cut in your skin. These cuts may possibly result in small scars.

The healthy volunteers will not personally benefit from participation in this study, but participation may contribute to further developments in treating brain infarction.

Contacts

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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. Males or non-pregnant, non-breastfeeding females, aged *18 and 65 years. Female subjects must be of non-childbearing potential, defined as pre-menopausal females with a documented tubal ligation, hysterectomy or bilateral oophorectomy; or as post-menopausal females defined as 12 months amenorrhea and follicle stimulating hormone (FSH) levels >40 IU/L.
2. Body mass index (BMI) *18 kg/m2 and 30 kg/m2 at screening.
3. A resting pulse *40 beats per minute (bpm) and *100 bpm at screening and on Day -1.
4. A resting systolic blood pressure of *150 mmHg and a resting diastolic blood pressure of *95 mmHg at screening and on Day -1.
5. Baseline laboratory test values within reference ranges based on the blood and urine samples taken at screening and on Day -1. Out of normal ranges values may be accepted by the Investigator, if not clinically significant. Values for hemostasis and coagulation blood test, for bleeding time and platelet aggregation should be normal.

Exclusion criteria

1. The subject has a history of hemorrhagic disease or venous or arterial thrombotic disease.
2. The subject has a history or presence of any disorder with an increased risk of bleeding

(e.g. ulcus pepticus, hemorrhoids).
3. The subject has used drugs modifying hemostasis or platelet function within the last month prior to administration of the study drug (i.e. aspirin, antiplatelet drugs, anti-vitamin K drugs and anticoagulant drugs).
4. The subject has used anti-histamines within the last month prior to administration of the study drug.
5. The subject has taken prescription or non-prescription medication, herbal remedies, vitamins or minerals within 2 weeks prior to administration of the study drug (or within 5 half-lives prior to administration of the study drug for any medication ingested, whichever is longer).

Study design

Design

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):	30-10-2017
Enrollment:	48
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	placebo
Generic name:	infusion bag 0.9% NaCl
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	04-10-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-10-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2017-003047-38-NL
CCMO	NL63251.056.17