A multi-centre, randomised, placebo controlled, double blinded, multiple dose trial investigating safety, pharmacokinetics and pharmacodynamics of concizumab administered subcutaneously to haemophilia A subjects

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Primary objective:- To assess the safety of concizumab given as multiple s.c. doses to subjects with haemophilia ASecondary objectives:- To assess pharmacokinetics of concizumab in subjects with haemophilia A after multiple s.c. doses- To assess…

Ethical review	Approved WMO
Status	Will not start
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON42365

Source
ToetsingOnline

Brief title
explorerTM3

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
blood clotting disorder, Haemophilia A

Research involving
Human

Sponsors and support

Primary sponsor: Novo Nordisk
Source(s) of monetary or material Support: Novo Nordisk (industrie)

Intervention

Keyword: Concizumab, Haemophilia A, Multiple dose, Subcutaneous administration

Outcome measures

Primary outcome

Primary endpoint:

- Number of adverse events (AEs) from first trial drug administration (day 1)

to 11 weeks after the first trial product administration.

Secondary outcome

Key secondary endpoints:

- Trough level of concizumab prior to the last subcutaneous dose administration

(day 42).

- Frequency of binding non-neutralizing anti-concizumab antibodies from first

trial drug administration (day 1) to 11 weeks after the first trial product

administration.

Study description

Background summary

Current replacement therapy of haemophilia with coagulation factors is hampered by the fact that these products must be given by intravenous injections. These injections are known to be painful, difficult, and time consuming for many patients resulting in delayed treatment or under-treated patients. In addition,

repeated venepuncture is not always possible in very young children. The use of an implantable venous access device has facilitated prophylaxis in some children, but is associated with complications such as infections, sepsis, and venous thrombosis. Therefore, a new therapeutic agent that can be administered subcutaneously will represent a major improvement in the treatment of haemophilia patients on prophylaxis.

Study objective

Primary objective:
- To assess the safety of concizumab given as multiple s.c. doses to subjects with haemophilia A

Secondary objectives:
- To assess pharmacokinetics of concizumab in subjects with haemophilia A after multiple s.c. doses
- To assess pharmacodynamics of concizumab in subjects with haemophilia A after multiple s.c. doses
- To assess immunogenicity of concizumab in subjects with haemophilia A

Study design

This phase I trial is designed as a randomised, placebo-controlled, double blinded within a cohort, multiple dose, dose escalation trial to investigate safety, pharmacokinetics (PK) and pharmacodynamics (PD) of concizumab when multiple doses are administered subcutaneously at five different concizumab dose levels in subjects with haemophilia A without inhibitors.
Five subcutaneous dose levels of concizumab (ranging from 0.25 to 1.5 mg/kg) are planned to be investigated. Each dose cohort will include 8 haemophilia subjects to be treated with concizumab/placebo in a 3:1 randomisation (6 subjects treated with concizumab and 2 subjects with placebo). The highest dose predicted to be given to trial subjects is 1.5 mg/kg.
Between each dose escalation, the population PK model will be updated with PK data from the previous cohort(s). The dose needed, to achieve the exposure level intended for the next ascending cohort, will be re-calculated and, if warranted, doses will be changed as appropriate. Thus, the trial design will allow for adjustment of dose levels based on an updated population PK model analysis of the exposure levels.
For each trial subject the trial consists of a minimum of 18 visits, including one screening visit (visit 1), visits in the dosing period (visit 2 to visit 13), visits in the follow-up period (visit 14 to visit 17) and one End of Trial (visit 18). A total of 12 doses of concizumab/placebo will be given to each trial subject over a 42 day period and the trial duration will be approximately 11 weeks. Every trial subject will receive his doses on day 1 and 2 followed by subsequent every fourth day.

Intervention

Trial products will be administered subcutaneously in the abdominal area under the surveillance of medically trained trial site staff on day 1 and 2, and subsequently every 4th day.

Study burden and risks

Occasionally, temporary discomfort, bruising, bleeding or swelling at the site of the needle insertion for withdrawal of the blood samples may occur. There is also a very small risk of infection at the place where the needle goes in your vein. In addition the use of trial product may cause side effects. There may be a risk of development of blood clots. To minimize the risk of development of blood clots, the trial will start with a very low dose leading to an exposure, which is not expected to significantly activate the blood clotting. Secondly, there may be a risk of development of antibodies against concizumab. Antibody responses have not been observed in the completed clinical trials, but may occur after longer exposure periods or when administered to a broader patient population. There may also be a risk of allergic reactions, including severe (anaphylactic) reactions, in connection with concizumab administration. Patients will be monitored closely on the occurrence of possible side effects or discomforts.
The extent of the burden and the risk associated with participation is necessary to collect enough data to be able to draw reliable conclusions.

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

- Male subjects diagnosed with haemophilia A without inhibitors present at screening and currently treated on-demand.
- Subjects with a baseline level of factor VIII * 2 % based on medical records.
- Age between 18 and 64 years both inclusive, at the time of signing informed consent
- Body weight between 50 and 100 kg, both inclusive.

Exclusion criteria

- Known or suspected hypersensitivity to trial product or related products.
- Platelet count below 50x10^9/L at screening.
- Any clinical signs or known history of thromboembolic events, or subjects considered at high risk of thromboembolic events as judged by the investigator.
- Subjects at increased risk of cardiovascular disease as judged by the investigator.

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:	Will not start
Enrollment:	3
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Nog niet bekend
Generic name:	concizumab

Ethics review

Approved WMO Date:	17-08-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2014-003793-16-NL
CCMO	NL53826.018.15