A Multi-centre, Single-blind Trial Evaluating Safety and Efficacy, including Pharmacokinetics, of NNC-0156-0000-0009 when used for Treatment and Prophylaxis of Bleeding Episodes in Patients with Haemophilia B

Published: 25-01-2011
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Primary Objective: To evaluate the immunogenicity of N9-GP.Key Secondary Objectives: * To evaluate clinical efficacy of haemostasis (treatment of bleeding episodes) of N9-GP.* To evaluate clinical efficacy of N9-GP in long term bleeding prophylaxis...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON36266

Source
ToetsingOnline

Brief title
Paradigm2

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
blood clotting disorder, Haemophilia B

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Haemophilia B, N9-GP, On-demand, Prophylaxis

Outcome measures

Primary outcome

Primary Endpoint: Incidence of inhibitory antibodies against FIX defined as

titre *0.6 BU.

Secondary outcome

Key Secondary Endpoints:

* Haemostatic effect of N9-GP when used for treatment of bleeding episodes,

assessed as success/failure based on a four-point scale for haemostatic

response (excellent, good, moderate and poor) by counting excellent and good as

success and moderate and poor as failure

* Number of bleeding episodes per patient during routine prophylaxis

* FIX trough levels

* Adverse Events (AEs) and Serious Adverse Events (SAEs)

* Host Cell Proteins (HCP)-antibodies

* General safety endpoints including laboratory parameters, physical

examination and vital signs

Study description

Background summary

The rationale for this pivotal trial is to investigate the safety and efficacy, including PK of N9-GP when used for treatment and prophylaxis of bleeding episodes in haemophilia B patients. Based on clinical and non-clinical studies conducted, N9-GP is a promising drug candidate for prevention/prophylaxis and on-demand treatment of bleedings in haemophilia B patients. The completed phase 1 trial showed a mean t* of 93 hours which is approximately 5 times higher than commercially available FIX concentrates.

Study objective

Primary Objective: To evaluate the immunogenicity of N9-GP.

Key Secondary Objectives:
* To evaluate clinical efficacy of haemostasis (treatment of bleeding episodes) of N9-GP.
* To evaluate clinical efficacy of N9-GP in long term bleeding prophylaxis (number of bleeding episodes during prophylaxis)
* To evaluate the efficacy of N9-GP by the surrogate marker for efficacy, FIX activity
* To evaluate general safety of N9-GP

Study design

The trial is a single-blind, multi-national trial evaluating safety, pharmacokinetics and clinical efficacy of N9-GP when used for treatment of bleeding episodes and for long-term prophylaxis. The trial therefore has characteristics of Phase 1, 2 and 3 (pharmacokinetics, safety and efficacy). Single-blind in this trial means that patients on prophylaxis do not know whether they are allocated to a low or high dose arm.

A minimum of 60 patients must complete the trial. The patients can be included in either the prophylaxis or the on-demand arm. In the prophylaxis arms the patients will be randomised to either a high dose arm or the low dose arm. Each patient in the prophylaxis arms must attain 50 exposure days to N9-GP through the trial.

Two PK profiles from 15 of the patients in the prophylaxis arms must be obtained during the trial and these PK sessions will be carried out with three different lots of N9-GP.

The duration of the trial for each patient in the prophylaxis arms will be 52

weeks, and for patients in the on-demand arm it will be 28 weeks.

Intervention

Weekly injections with N9-GP (prophylaxis) or injections with N9-GP at the first signs of a bleeding episode (on-demand).

Study burden and risks

It's possible that bloodwithdrawals or injections with N9-GP can cause haemorrhages or discomfort. There is also a very small chance of infection on the injection site. The patient could also experience side effects from N9-GP. There is a risk of development of antibodies against N9-GP and/or FIX that could decrease the effectiveness of future treatments with FIX products.

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 patients, aged 13-70 years, with moderately severe or severe congenital haemophilia B with a FIX activity *2% according to medical records
NB: In The Netherlands only patients aged 18-70 years will be included
* History of at least 150 exposure days to other FIX products
* Patients currently treated on-demand with at least 6 bleeding episodes during the last 12 months or at least 3 bleeding episodes during the last 6 months, or patients currently on prophylaxis

Exclusion criteria

* Known history of FIX inhibitors based on existing medical records, laboratory report reviews and patient and LAR interviews
* Current FIX inhibitors *0.6 BU (central laboratory)
* HIV positive with a viral load *400,000 copies/mL and/or CD4+ lymphocyte count *200/*L
* Congenital or acquired coagulation disorders other than haemophilia B
* Previous arterial thrombotic events (e.g. myocardial infarction and intracranial thrombosis) or previous deep venous thrombosis or pulmonary embolism (as defined by available medical records)
* Platelet count <50.000 platelets/*l at screening (local laboratory)
* ALT >3 times the upper limit of normal reference ranges at screening (central laboratory)
* Creatinine level *1.5 times above upper normal limit at screening (central laboratory)
* Immune modulating or chemotherapeutic medication

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-10-2011
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Not yet known
Generic name:	N9-GP

Ethics review

Approved WMO Date:	25-01-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	18-05-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-07-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	27-12-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-01-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO	

Date:	17-04-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2010-023069-24-NL
ClinicalTrials.gov	NCT01333111
CCMO	NL35181.041.11