Safety and Efficacy of NNC-0156-0000-0009 after Long-Term Exposure in Patients with Haemophilia B

Published: 25-01-2011
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Primary Objective: To evaluate the immunogenicity of N9-GPKey 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-OMON39320

Source
ToetsingOnline

Brief title
paradigm*4

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: Extension, Haemophilia B, N9-GP, Trial

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 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 during routine prophylaxis

* FIX trough levels

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

* General safety endpoints including laboratory parameters, physical

examination and vital signs

Study description

Background summary

The rationale for this extension trial is to investigate the safety and efficacy of long-term treatment with N9-GP in haemophilia B patients. This is in accordance with the EMA guideline. 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 efficacy of N9-GP by the surrogate marker for efficacy, FIX activity
* To evaluate general safety of N9-GP

Study design

The trial is designed as an open, non-randomised, multi-national trial with the purpose of evaluating safety and clinical efficacy of treatment of bleeding episodes and for long-term prophylaxis with N9-GP.

A minimum of 50-100 patients are planned to complete the trial. The trial will have one treatment arm with four different treatment regimens: three prophylaxis treatment regimens and one on-demand treatment.

After completion of either the pivotal trial (Paradigm2), or the surgery trial (Paradigm3) patients may be offered to continue with prophylaxis or on-demand treatment in this phase 3b extension trial until no later than 31 March 2014.

Patients eligible for the trial will receive N9-GP as prophylaxis or as on-demand treatment. The choice of treatment is agreed between the patient and the Investigator and can be changed through the trial. However, with Substantial Amendment no 17 change of treatment regime is no longer possible for patients treated on demand or with the low weekly prophylaxis dose (10 U/kg).
In most cases, N9-GP is administered at home except when patients on prophylaxis are attending a visit at the clinic. In this case, N9-GP is administered at the clinic to allow for both pre- and post-dose blood samples and assessments. The patients will initially attend the clinic every 3 months, reducing to every 6 months after Visit 5.

Intervention

Weekly injections with N9-GP (prophylaxis), every second week 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

Previous participation in Paradigm2 or Paradigm3

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
* 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)
* Any disease (liver, kidney, inflammatory and mental disorders included) or condition which, according to the Investigator*s judgement, could imply a potential hazard to the patient, interfere with trial participation, or interfere with trial outcome

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-10-2012
Enrollment:	3
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:	25-08-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	13-09-2011
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:	15-02-2012
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)
Approved WMO Date:	22-03-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-04-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-08-2013

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-10-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-10-2013
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	EUCTR2010-023072-17-NL
ClinicalTrials.gov	NCT01395810
CCMO	NL35226.041.11