A Multi-national Trial Evaluating Safety and Efficacy, including Pharmacokinetics, of NNC 0129-0000-1003 (N8-GP) when Administered for Treatment and Prophylaxis of Bleeding in Patients with Haemophilia A

Published: 14-11-2011
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Co-Primary Objectives* To evaluate the immunogenicity of N8-GP in previously treated patients with haemophilia A* To evaluate the clinical efficacy of N8-GP in bleeding prohylaxis (number of bleeds during prophylaxis)Secondary Objectives* To...

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

Summary

ID

NL-OMON43797

Source
ToetsingOnline

Brief title
pathfinder* 2

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
blood clothing disorder, Haemophillia A

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Haemophilia A, N8-GP, On-demand, Prophylaxis

Outcome measures

Primary outcome

Co-Primary Endpoints

* The Incidence rate of FVIII-inhibitors *0.6 BU

* Annualised bleeding rate for patients receiving prophylaxis treatment

Secondary outcome

Secondary Endpoints

* Haemostatic effect of N8-GP when used for treatment of bleeds, assessed on a four-point scale for haemostatic response (excellent, good, moderate and none) by counting excellent and good as success and moderate and none as failure

* Consumption of N8-GP (number of infusions and U/kg) per bleed

* Consumption of N8-GP (number of infusions and U/kg per month and per year) during prophylaxis and on-demand treatment

* Haemostatic effect as measured by recovery and trough levels Factor VIII (in all patients receiving prophylaxis treatment)

* Patient Reported Outcomes and Health Economic outcomes

* Adverse Events (AEs) and Serious Adverse Events (SAEs) reported during the trial

* Changes in vital signs (BP, pulse, temperature, respiratory rate)

* Pharmacokinetic Outcomes

Study description

Background summary

The rationale for this trial is to investigate the safety and efficacy, including PK and long-term safety of N8-GP when used for treatment and prophylaxis of bleeding episodes in haemophilia A patients. One phase 1 trial has been completed with 26 PTPs dosed with N8-GP and had undergone a safety and PK investigation. The phase 1 trial has successfully been concluded with no safety concerns.

Study objective

Co-Primary Objectives
* To evaluate the immunogenicity of N8-GP in previously treated patients with haemophilia A
* To evaluate the clinical efficacy of N8-GP in bleeding prohylaxis (number of bleeds during prophylaxis)

Secondary Objectives
* To evaluate the clinical efficacy of N8-GP when treating bleeds in patients with haemophilia A
* To evaluate the safety of N8-GP when used for prevention of bleeds and treatment of bleeds in patients with heamophilia A
* To evaluate PK properties of N8-GP
* To evaluate Patient Reported Outcomes (PRO)
* To evaluate the health economic impact of N8-GP treatment
* Generation of a population based PK-model for N8-GP

Study design

This phase 3 trial is a multi-centre, multi-national, open-label, non-randomised trial evaluating safety, pharmacokinetics and clinical efficacy of N8-GP when used for treatment of bleeding episodes and for long-term prophylaxis.
A minimum of 155 patients must complete the Main Phase of the trial including at least 10 patients in on-demand treatment and 145 patients in prophylaxis treatment with N8-GP every 4 days.
A minimum of 15 of the patients in the prophylaxis arm must undergo 2 PK sessions.

Treatment duration in the Main Phase is approximately 7-19 months. All patients will continue in the trial until the last patient has received at least 50 exposure days of N8-GP. In this way a considerable portion of the patients will be treated prophylactic with N8-GP for more than 1 year.
When the Main Phase of the trail has completed, all patients will be offered to continue treatment in the Extension Phase of the trial. The extension trial is designed to obtain long-term safety and efficacy data for prophylactic treatment every 4 days or every 7 days, and for on-demand treatment.

Intervention

Injections with N8-GP every 4 days (prophylaxis) and/or injections with N8-GP at the first signs of a bleeding episode (on-demand).
In the Extension Phase it is also possible to have injections with N8-GP every 7 days as prophylaxis.

Study burden and risks

It's possible that bloodwithdrawals or injections with N8-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 N8-GP. There is a risk of development of antibodies against N8-GP and/or Factor VIII that could decrease the effectiveness of future treatments with Factor VIII 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 with severe congenital haemophilia A (FVIII activity <1%, according to medical records)
- Documented history of at least 150 EDs to other FVIII products
- Age * 12 years and body weight * 35 kg (except for Croatia, The Netherlands, France, Russia and Israel where the lower age limit will be 18 years)

Exclusion criteria

- Previous participation in this trial defined as withdrawal after administration N8-GP
- Any history of FVIII inhibitors
- FVIII inhibitors * 0.6 BU/mL at screening
- HIV positive, defined by medical records with CD4+ count *200/µL or a viral load of >400000 copies/mL If the data is not available in medical records within last 6 months, CD4+ will be measured at the screening visit
- Congenital or acquired coagulation disorders other than haemophilia A
- Previous significant thromboembolic events (e.g. myocardial infarction, cerebrovascular disease or deep venous thrombosis) as defined by available medical records
- Platelet count < 50,000 platelets/µL (laboratory value at the screening visit)
- ALAT > 3 times the upper limit of normal reference ranges at central laboratory
- Creatinine level * 1.5 times above upper normal limit (according to central laboratory reference ranges)
- Ongoing immune modulating or chemotherapeutic medication

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):	03-07-2012
Enrollment:	7
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Not yet known
Generic name:	N8-GP

Ethics review

Approved WMO

Date:	14-11-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	13-02-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	14-05-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	15-06-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-12-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-01-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-05-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-11-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-12-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	28-03-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-04-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-10-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-11-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-12-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-06-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-08-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-12-2016

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-02-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-04-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-11-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-11-2017
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	EUCTR2011-001142-15-NL
ClinicalTrials.gov	NCT01480180
CCMO	NL38625.078.11