Safety and Efficacy of nonacog beta pegol (N9-GP) in Previously Untreated Patients with Haemophilia B

Published: 23-07-2015
Last updated: 19-04-2024

Primary Objective- To evaluate immunogenicity of N9-GP (nonacog beta pegol)Secondary Objectives- To evaluate safety of N9-GP (nonacog beta pegol)- To evaluate efficacy of N9-GP (nonacog beta pegol) * in long-term prophylaxis treatment * in the...

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

Summary

ID

NL-OMON50546

Source
ToetsingOnline

Brief title
paradigm*6

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
Haemophilia B / blood clotting disorder

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, PUP

Outcome measures

Primary outcome

Primary Endpoint

• Incidence of inhibitory antibodies against FIX

Secondary outcome

Key Secondary Endpoint

• Number and frequency of adverse events, serious adverse events, and Medical

Events of Special Interest

• Number of breakthrough bleeding episodes during prophylaxis (annualised

bleeding rate)

• Haemostatic effect by 4-point haemostatic response scale (*excellent*,

good, *moderate* and *poor*)

Study description

Background summary

Children are among those who might benefit significantly from prophylaxis with N9-GP. The most commonly used products for the treatment of haemophilia B have short half-life of 18 19 hours demanding frequent dosing for prophylaxis of bleeding episodes, with 2-3 injections a week. The prolonged half-life of N9-GP offers an expected advantage of once weekly or potentially even less frequent injections, which reduces the burden of treatment while maintaining effective haemostasis. Likewise it may promote adherence to therapy due to less frequent injections. The pivotal phase 3 trial (NN7999-3747) demonstrated a prophylactic protection of 40 IU/kg N9-GP once weekly and showed that 99% of bleeding episodes in the 40 IU/kg arm were stopped with a single dose of N9-GP. Furthermore EMA requires separate investigation of PUPs as part of the development programme initiated before market authorisation (MA) gets obtained.

A final guideline on the clinical investigation of recombinant and human plasma-derived factor IX products from the Committee for Medical Product for Human Use (CHMP), describes the mandatory components for trials in PUP. In some countries outside the EU, PUP Paediatric investigation is necessary to achieve labelled indication for all children.

Study objective

Primary Objective
- To evaluate immunogenicity of N9-GP (nonacog beta pegol)

Secondary Objectives
- To evaluate safety of N9-GP (nonacog beta pegol)

- To evaluate efficacy of N9-GP (nonacog beta pegol)
* in long-term prophylaxis treatment
* in the treatment of bleeding episodes
* through the surrogate marker: FIX activity
* through monitoring of number of doses and consumption of N9-GP

Study design

The trial is an open label, single-arm, multinational, non-controlled confirmatory trial investigating safety and efficacy of N9-GP in prophylaxis and treatment of breakthrough bleeding episodes in haemophilia B previously untreated patients with FIX activity <= 2%.The trial has one treatment arm in which at least 40 patients should achieve 100 exposure days with N9-GP.
The European medicines agency requires submission of safety and efficacy data from a minimum of 50 exposure days in at least 20 patients for approval of the indication in previously untreated patients, with a post-approval extension phase according to guideline to follow-up in at least 40 patients, for a minimum of 100 exposure days. When the first 20 patients have reached at least 50 exposure days, the analysis and evaluation for the main trial report will be performed. All patients continue in the extension phase for the purpose of acquiring data for a minimum of 100 exposure days in at least 40 patients.

Intervention

Injection of 40 IU/kg N9-GP administered every 7th day to prevent bleeding episodes, and in addition immediate treatment with 40 IU/kg N9-GP in case of a mild or moderate bleeding or 80 IU/kg in case of a severe bleeding episode.

Study burden and risks

Occasionally, temporary discomfort, bruising, bleeding or swelling at the site of needle insertion for the withdrawal of the blood samples or trial medicine

injection may occur. There is also a very small risk of infection at the place where the needle goes into your son*s vein.
There is also a risk of side effects. The primary concern in PUPs is the risk of development of neutralizing antibodies to FIX (inhibitors). Development of binding antibodies and inhibitors will be monitored closely throughout the trial.
Hypersensitivity reactions may occur with the administration of N9-GP, as with any protein injected intravenously. Patients will be closely monitored for development of hypersensitivity reactions, in relation to the first 20 exposures with N9-GP.
No unexpected safety issues have been identified in the completed and ongoing clinical trials with N9-GP and the risk/benefit ratio for N9-GP is therefore expected to be favorable.

Contacts

Public
Novo Nordisk

Flemingweg 8
Alphen a/d Rijn 2408 AV
NL
Scientific
Novo Nordisk

Flemingweg 8
Alphen a/d Rijn 2408 AV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

- Informed consent obtained before any trial-related activities. Trial-related activities are any procedures that are carried out as part of the trial, including activities to determine suitability for the trial, - Male, < 6 years of age at the time of signing informed consent, - Patients with the diagnosis of haemophilia B (FIX activity level <= 2%) based on medical records or central laboratory results, - Previously untreated or exposed to FIX containing products less than or equal to 3 exposure days (5 previous exposure days to blood components are acceptable)

Exclusion criteria

- Any history of FIX inhibitors (defined by medical records), - Known or suspected hypersensitivity to trial product or related products, - Previous participation in this trial. Participation is defined as first dose administered of trial product, - Receipt of any investigational medicinal product within 30 days before screening, - Congenital or acquired coagulation disorder other than haemophilia B, - Any chronic disorder or severe disease which, in the opinion of the Investigator, might jeopardise patient*s safety or compliance with the protocol, - Patient*s parent(s)/LAR(s) mental incapacity, unwillingness to cooperate, or a language barrier precluding adequate understanding and cooperation

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-07-2014

Enrollment:	1
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Refixia
Generic name:	recombinant factor IX

Ethics review

Approved WMO Date:	23-07-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-05-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-12-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-01-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-03-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-03-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	29-06-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-07-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-10-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-11-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-03-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-07-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-07-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-08-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	12-08-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-09-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-10-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-01-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-01-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2012-004867-38-NL
ClinicalTrials.gov	NCT02141074

Register	ID
CCMO	NL53683.091.15