An Open-Label, Multicenter Evaluation of the Safety and Efficacy of Recombinant Coagulation Factor IX Fc Fusion Protein (rFIXFc; BIIB029) in the Prevention and Treatment of Bleeding in Previously Untreated Patients With Severe Hemophilia B

Published: 28-08-2014
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The purpose of this study is to investigate the safety and efficacy of rFIXFc in previously untreated patients (PUPs) in accordance with the European Medicines Agency Committee for Medicinal Products for Human Use (CHMP) guideline on clinical...

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

Summary

ID

NL-OMON47235

Source
ToetsingOnline

Brief title
998HB303, PUPs B

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Blood and lymphatic system disorders congenital

Synonym

Hemophilia, Hemophilia B

Research involving
Human

Sponsors and support

Primary sponsor: Bioverativ Therapeutics Inc.
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Efficacy, Hemophilia B, rFIXFc, Safety

Outcome measures

Primary outcome

The primary objective of the study is to evaluate the safety of rFIXFc in

previously untreated subjects with severe hemophilia B.

Secondary outcome

The secondary objectives of the study are as follows:

To evaluate the efficacy of rFIXFc in the prevention and treatment of bleeding

episodes in PUPs.

To evaluate rFIXFc consumption for prevention and treatment of bleeding

episodes in PUPs.

Study description

Background summary

The use of a prophylaxis regimen in young children starting prior to the onset of frequent joint bleeding is currently the recommended standard of care in hemophilia due to the demonstrated benefit on long-term outcomes replacement therapies are limited by short elimination half-life requiring intravenous administration up to 3 times per week.

Study objective

The purpose of this study is to investigate the safety and efficacy of rFIXFc in previously untreated patients (PUPs) in accordance with the European Medicines Agency Committee for Medicinal Products for Human Use (CHMP) guideline on clinical investigation of recombinant and human plasma-derived factor IX products.

Study design

An open-label, single-arm, multicenter study evaluating the safety and efficacy of rFIXFc in previously untreated subjects with severe hemophilia B when used according to local standard of care for implementation of a prophylaxis regimen, including an optional preceding episodic (on-demand) treatment regimen. Following the Baseline Visit, the Investigator has the option to treat the subject episodically before initiating a prophylaxis regimen. The duration of episodic treatment is at the Investigator*s discretion, in accordance with local standard of care. The study will end when at least 40 subjects have reached at least 100 EDs with rFIXFc. Surgery is allowed during the study. Immune tolerance induction with rFIXFc is allowed during the study for those subjects developing a positive inhibitor after exposure to rFIXFc study drug. Adjustments to the dose and interval of rFIXFc can be made in this study based on available pharmacokinetic (PK) data, subsequent FIX trough and peak levels, level of physical activity, and bleeding pattern, in accordance with local standards of care for a prophylactic regimen.

Intervention

Following the Baseline Visit, the Investigator has the option to treat the subject episodically before initiating a prophylaxis regimen.

Episodic (on-demand) treatment is permitted; starting after the Baseline Visit and lasting until a prophylactic regimen is initiated. Dosing will be determined by the Investigator using Appendix A as a guideline. The duration of episodic treatment should be based upon the Investigator*s treatment plan for the subject in accordance with local standards.

The recommended initial prophylactic regimen is 50 IU/kg weekly. Adjustments to the dose and dosing interval can be made based upon available incremental recovery data (see Section 10.1.1), subsequent FIX trough and peak levels, level of physical activity and bleeding pattern, in accordance with local standards of care for a prophylactic regimen. Treatment will continue until the subject has reached at least 100 EDs to rFIXFc study drug.

rFIXFc will be delivered by IV injection over 5 (±5) minutes; the rate of administration should be determined by the subject*s comfort level.

Study burden and risks

rFIXFc can cause side effects and as with any new drug, there is a risk of rare or previously unknown side effects, including cancer risks, allergy risks and/or a chance that rFIXFc might interact with other drugs.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. Ability of the subject or their parent or legal guardian to understand the purpose and risks of the study and provide signed and dated informed consent and authorization to use protected health information (PHI) or equivalent, and/or to provide assent in accordance with national and local regulations.;2. Male, age <18 years at the time of informed consent.;3. Weight *3.5 kg at the time of informed consent.;4. Severe hemophilia B defined as *2 IU/dL (*2%) endogenous FIX documented in the medical record or as tested during the Screening

Period. Any subject who is enrolled based on results of the local laboratory must be withdrawn if the central laboratory screening results indicate a baseline FIX activity level >2% of normal.

Exclusion criteria

1. History of positive inhibitor testing. A prior history of inhibitors is defined based on a patient's historical positive inhibitor test using the local laboratory Bethesda value for a positive inhibitor test (i.e. equal to or above lower limit of detection).
2. History of hypersensitivity reactions associated with any rFIXFc administration.
3. Exposure to blood components or injection with a FIX concentrate (including plasma derived) other than rFIXc.
4. Injection with commercially available rFIXFc more than 28 days prior to Screening.
5. More than 3 injections of commercially available rFIXFc prior to confirmation of eligibility.
6. Other coagulation disorder(s) in addition to hemophilia B.
7. Any concurrent clinically significant major disease that, in the opinion of the Investigator, would make the subject unsuitable for enrollment (e.g., HIV infection with CD4 lymphocyte count <200 cells/µL or a viral load > 200 particles/µL, or any other known congenital or acquired immunodeficiency).
8. Current systemic treatment with chemotherapy and/or other immunosuppressant drugs. Use of steroids for treatment of asthma or management of acute allergic episodes or otherwise life-threatening episodes is allowed. Treatment in these circumstances should not exceed a 14-day duration.
9. Participation within the past 30 days in any other clinical study involving investigational treatment.
10. Current enrollment in any other clinical study involving investigational treatment.
11. Inability to comply with study requirements.
12. Other unspecified reasons that, in the opinion of the Investigator or Bioverativ, make the subject unsuitable for enrollment.

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):	11-05-2015
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alprolix
Generic name:	recombinant Factor IX-Fc

Ethics review

Approved WMO Date:	28-08-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-12-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-11-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-12-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-07-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	27-07-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-06-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-07-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-09-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-10-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-11-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-11-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-12-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-06-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	04-09-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-10-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-01-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2013-003629-27-NL
ClinicalTrials.gov	NCT02234310
CCMO	NL49000.042.14