An Open-Label, Multicenter Evaluation of the Safety and Efficacy of Recombinant Coagulation Factor VIII Fc Fusion Protein (rFVIIIFc; BIIB031) in the Prevention and Treatment of Bleeding in Previously Untreated Patients With Severe Hemophilia A

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON45745

Source
ToetsingOnline

Brief title
997HA306, PUPs A (ALONG)

Condition

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

Synonym

Hemophilia, Hemophilia A

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Efficacy, Hemophilia A, rFVIIIFc, Safety

Outcome measures

Primary outcome

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

previously untreated subjects with severe hemophilia A.

The primary endpoint of the study is the occurrence of inhibitor development.

Secondary outcome

Secondary objectives are as follows**

* To evaluate the efficacy of rFVIIIFc in the prevention and treatment of

bleeding episodes in PUPs

* To evaluate rFVIIIFc consumption for the prevention and treatment of bleeding

episodes in PUPs

* To describe experience with the use of rFVIIIFc for immune tolerance

induction (ITI) in subjects with inhibitors

The exploratory objective is to evaluate the effect of rFVIIIFc based on

patient-reported outcomes and health resource utilization.

The secondary endpoints of the study are as follows:

* The annualized number of bleeding episodes per subject

* The annualized number of spontaneous joint bleeding episodes per subject

* The number of injections and dose per injection of rFVIIIFc required to

resolve a bleeding episode

* Assessments of response to treatment with rFVIIIFc for bleeding episodes,

using the 4-point bleeding response scale

* The total number of exposure days (EDs) per subject per year

* Total annualized rFVIIIFc consumption per subject for the prevention and

treatment of bleeding episodes

* rFVIIIFc incremental recovery (IR)

* Response to ITI with rFVIIIFc (success, partial success, failure, early

withdrawal)

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. Currently available coagulation factor VIII (FVIII) replacement therapies are limited by short elimination half-life (t*).

Study objective

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

Study design

An open-label, single-arm, multicenter study evaluating the safety and efficacy of rFVIIIFc in previously untreated pediatric subjects with severe hemophilia A when used according to local standard of care for implementation of a prophylaxis regimen, including an optional preceding episodic (on-demand) treatment regimen. The duration of episodic treatment is at the Investigator*s discretion, in accordance with local standard of care.
Subjects actively bleeding and requiring emergent treatment may be enrolled and receive study drug after samples for inhibitor testing at the central laboratory have been obtained, with results pending. However any such subject must be withdrawn if the central laboratory screening results indicate a positive inhibitor.
The study will end when at least 100 subjects have reached at least 100 EDs with rFVIIIFc. Surgery is allowed during the study. ITI is allowed during the study for subjects developing a positive inhibitor after exposure to rFVIIIFc. Separate consent/assent is required before starting an ITI regimen.

Intervention

The Baseline Visit assessments should be performed as soon as practicable once all eligibility criteria have been met.

Following the Baseline Visit, the Investigator has the option to treat the subject with an episodic regimen for a period of time before initiating a prophylaxis regimen. The duration of the episodic period is at the Investigator*s discretion, in accordance with local standard of care. However, given global standards of care, it is expected that the prophylactic regimen will be initiated prior to or immediately following a third episode of hemarthrosis

The dose for initiation of prophylaxis may be chosen by the Investigator within the range of 20 to 80 IU/kg. Based on data from the completed clinical studies, and knowledge of increased clearance of factor concentrates in children <6 years of age, doses of up to 80 IU/kg every 3 to 4 days may be required to minimize breakthrough bleeding events. Alternatively, lower doses of 25 to 50 IU/kg every 2 days can be used. Adjustments to the dose and interval of rFVIIIFc can be made in this study based on available PK data, subsequent FVIII 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 rFVIIIFc (or until end of study is declared). Parents/caregivers, or children capable of self-injection, will be instructed to administer rFVIIIFc at home.

Beginning with the Baseline Visit, subjects will visit the clinic every 12 (±2)

weeks by calendar date.
In addition to scheduled clinic visits, telephone calls are planned approximately once a month for study site staff to check on each subject*s status. Additional unscheduled visits may be necessary during the study to test for inhibitors, test for recovery, repeat safety assessments, repeat any blood sampling if required for study purposes or for local standard of care, or perform PK assessments if needed for surgical planning or adjustment of dosing regimen.

Study burden and risks

Like all medicines, rFVIIIFc can cause side effects, although not everybody gets them. Possible side effects are described in the Investigators Brochure.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1.Ability of the subject or his 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) in accordance with national and local subject privacy regulations. Subjects may provide assent in addition to the parental/guardian consent, if appropriate.;2. Male, age <6 years at the time of informed consent.;3. Weight *3.5 kg ;4. Severe hemophilia A defined as <1 IU/dL (<1%) endogenous FVIII 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 FVIII activity level *1% of normal.

Exclusion criteria

1. Prior history of inhibitor as defined by the reporting laboratory. The historical positive inhibitor test is defined as per local laboratory Bethesda value for a positive inhibitor test (i.e., equal to or above lower level of detection).;2. Measurable inhibitor activity at the Screening Visit, measured using the Nijmegen-modified Bethesda assay performed at the central laboratory. A negative inhibitor test result at the local laboratory may be used initially to determine subject eligibility; however, any subject who is enrolled based on results of the local laboratory must be withdrawn if the central laboratory screening results indicate a positive inhibitor. Subjects actively bleeding and requiring emergent treatment may be enrolled and receive study drug after samples for inhibitor testing at the central laboratory have been obtained, with results pending. However, any such subject must be withdrawn if the central laboratory screening results indicate a positive inhibitor.;3. History of hypersensitivity reactions associated with any IV immunoglobulin administration.;4. Injection with any FVIII replacement product or any blood component prior to confirmation of eligibility.;5. Injection with rFVIIIFc prior to confirmation of eligibility.;6. Other coagulation disorder(s) in addition to hemophilia A.;7. Any concurrent clinically significant major disease that, in the opinion of the Investigator, would make the subject unsuitable for enrollment.;8. Current systemic treatment with chemotherapy and/or other immunosuppressant drugs. Use of corticosteroids for the treatment of asthma or management of acute allergic episodes is allowed with the exception of systemic corticosteroid treatment given to children daily or on alternate days at *2 mg/kg per day of prednisone or its equivalent or *20 mg/day if they weigh more than 10 kg with a duration of longer than 14 days.;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 Biogen Idec, 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:	Will not start
Enrollment:	4
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Elocta
Generic name:	recombinant Factor VIII-Fc
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	15-06-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-10-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-12-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-02-2017

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-06-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-06-2017
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:	05-10-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-11-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-01-2018
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	EUCTR2013-005512-10-NL
ClinicalTrials.gov	NCT02234323
CCMO	NL56493.042.16