A Phase 3 open-label, multicenter study of the safety, efficacy, and pharmacokinetics of intravenous recombinant coagulation Factor VIII Fc-von Willebrand Factor-XTEN fusion protein (rFVIIIFc-VWF-XTEN; BIVV001) in previously treated pediatric patients <12 years of age with severe hemophilia A

Published: 18-11-2020
Last updated: 09-04-2024

To evaluate the safety of BIVV001 in previously treated pediatric subjects with hemophilia A.

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

Summary

ID

NL-OMON49869

Source
ToetsingOnline

Brief title
XTEND-Kids

Condition

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

Synonym
hemophilia A

Research involving
Human

Sponsors and support

Primary sponsor: Genzyme Europe BV
Source(s) of monetary or material Support: Bioverativ Therapeutics Inc.

Intervention

Keyword: children, Hemophilia A, open-label, phase 3

Outcome measures

Primary outcome

Occurrence of inhibitor development

Secondary outcome

- Annualized bleeding rate (ABR), ABR by type of bleed and ABR by location of bleed

- Percentage of participants who maintain FVIII activity above prespecified levels

- Number of injection and dose of BIVV001 to treat a bleeding episode

- Percentage of bleeding episodes treated with a single injection of BIVV001

- Assessment of response to BIVV001 treatment of individual bleeding episodes

- Physician*s global assessment of the participant*s response based on BIVV001 treatment

- Total annualized BIVV001 consumption

- Annualized Joint Bleeding Rate (AJBR)

- Target joint resolution

- Change in Hemophilia Joint Health Score (HJHS) total score and domain scores

- Changes in Haemophilia Quality of Life Questionnaire for Children (Haemo-QoL) total score and physical health domain scores from baseline to week 52

- Investigators* or Surgeons* assessment of participant*s hemostatic response to BIVV001 treatment

- Number of injections and dose to maintain hemostasis during perioperative period for major surgery

- Total BIVV001 consumption during perioperative period for major surgery

- Number of blood component transfusions used during perioperative period for major surgery

- Type of blood component transfusions used during perioperative period for major surgery

- Estimated blood loss during perioperative period for major surgery

- Number of participants with occurence of adverse events (AEs) and serious adverse events (SAEs)

- Number of participants with occurrence of embolic and thrombotic events

- PK parameter: Maximum activity (Cmax), elimination half-life (t1/2), total clearance (CL), total clearance at steady state (CLss), dose-normalized area under the activity-time curve (DNAUC), area under the activity time curve (AUC), volume of distribution at steady state (Vss), mean residence time (MRT), incremental recovery (IR), trough activity (Ctrough), time above predefined FVIII activity levels

Study description

Background summary

Hemophilia A is a congenital X-linked bleeding disorder that occurs predominantly in males and is characterized by deficiency of functional FVIII. Individuals with severe hemophilia experience frequent bleeding episodes into major joints, soft tissue, and muscle, either spontaneously or following minor trauma. The disease can be acutely life-threatening. Repeated bleeding can lead to debilitating long-term complications, including hemophilic arthropathy from bleeding into the joints.

BIVV001 is designed to be a new class of blood clotting FVIII. Preclinical and clinical experience indicate that BIVV001 has an extended half-life, which can achieve and maintain higher sustained factor activity levels than currently available treatments, with less frequent administration.

Study objective

To evaluate the safety of BIVV001 in previously treated pediatric subjects with hemophilia A.

Study design

Phase 3, open label, single arm.

Intervention

Weekly dose (intravenous) of BIVV001 for 52 weeks.

Study burden and risks

The risks are related to the blood sampling and possible side effects of the study drug.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

- Participant must be younger than 12 years of age, at the time of signing the informed consent
- Severe hemophilia A defined as <1 IU/dL (<1%) endogenous FVIII as documented either by central laboratory testing at Screening or in historical medical records from a clinical laboratory demonstrating <1% FVIII coagulant activity (FVIII:C) or a documented genotype known to produce severe hemophilia A.
- Previous treatment for hemophilia A (prophylaxis or on-demand) with any recombinant and/or plasma-derived FVIII, or cryoprecipitate for at least 150 EDs for patients aged 6-11 years and above 50 EDs for patients aged below 6 years
- Weight above or equal to 10 kg.

Exclusion criteria

- History of hypersensitivity or anaphylaxis associated with any FVIII product.
- History of a positive inhibitor (to FVIII) test defined as >=0.6 BU/mL, or any value greater than or equal to the lower sensitivity cut-off for laboratories with cut-offs for inhibitor detection between 0.7 and 1.0 BU/mL, or clinical signs or symptoms of decreased response to FVIII administrations. Family history of inhibitors will not exclude the participant.

- Positive inhibitor test result, defined as >=0.6 BU/mL at Screening.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	22-02-2021
Enrollment:	3
Type:	Anticipated

Ethics review

Approved WMO Date:	18-11-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-01-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	06-05-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-08-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-10-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-01-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	25-05-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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	EUCTR2020-000769-18-NL
Other	na
CCMO	NL74679.018.20