A Phase 3 open-label, multicenter study of the long-term safety and efficacy of intravenous recombinant coagulation factor VIII Fc-von Willebrand factor-XTEN fusion protein (rFVIIIFc-VWF-XTEN; BIVV001) in Previously Treated Patients with severe hemophilia A

Published: 26-05-2021
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This study has been transitioned to CTIS with ID 2023-508929-27-00 check the CTIS register for the current data. -To evaluate the long-term safety of BIVV001 in previously treated patients with hemophilia A.-To evaluate the efficacy of BIVV001 as a…

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

Summary

ID

NL-OMON54275

Source
ToetsingOnline

Brief title
LTS16294/ XTEND-ed

Condition

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

Synonym

Hemophilia A

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Hemophilia A, Open-label, Phase 3

Outcome measures

Primary outcome

The occurrence of inhibitor development (neutralizing antibodies directed

against FVIII)

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 (Haemo-QoL) total score and physical health domain scores from baseline to end of study for maximum 4 years

- 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

This study has been transitioned to CTIS with ID 2023-508929-27-00 check the CTIS register for the current data.

-To evaluate the long-term safety of BIVV001 in previously treated patients with hemophilia A.
-To evaluate the efficacy of BIVV001 as a prophylaxis treatment.

Study design

Phase 3, open label, long-term safety and efficacy, 3 treatment arms (A, B and C)

Intervention

Weekly administration (intravenous) of BIVV001 for a maximum period of 4 years.

Study burden and risks

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

Contacts

Public

Sanofi BV

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

For Arm A
- Ability 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 participant privacy regulations. Parents or legal
guardians* consent is required for participants who are <18 years of age or unable to give
consent, or as applicable per local laws. Participants who are <18 years of age may provide
assent in addition to the parents/legal guardians consent, if appropriate.
- Participants who have completed the studies EFC16923, EFC16925, Arm B or Arm C of

the current study, or any other potential BIVV001 study.
- Male or female: Contraceptive use by men or women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.
- Willingness and ability of the participant or surrogate (a caregiver or a family member
>=18 years of age) to continue use of the study ePD throughout the study.

For Arm C
- Participants who have severe hemophilia A, defined as <1 IU/dL (<1%) endogenous FVIII
activity 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 or 50 EDs for
participants aged <6 years.
- Platelet count >=100 000 cells/µL at screening.
- Weight above or equal to 10 kg.

Arm B is only applicable for China

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. Any concurrent clinically significant liver disease.
- Serious active bacterial, fungal, or viral infection.
- Other known coagulation disorder(s) in addition to hemophilia A.
- Abnormal renal function or significant liver disease.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-10-2021
Enrollment:	4
Type:	Actual

Ethics review

Approved WMO Date:	26-05-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-08-2021
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:	10-01-2023
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:	18-01-2023
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:	02-05-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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Approved WMO Date:	26-05-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	05-07-2023
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
EU-CTR	CTIS2023-508929-27-00
EudraCT	EUCTR2020-002215-22-NL
CCMO	NL75430.018.21