A prospective, lead-in study to collect bleeding episodes, Factor VIII (FVIII) infusions, and patient-reported outcomes in patients with hemophilia A

Published: 01-07-2021
Last updated: 05-04-2024

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

Summary

ID

NL-OMON51102

Source
ToetsingOnline

Brief title
Get-8 Lead In

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
bleeding disorder, hemophila A

Research involving
Human

Sponsors and support

Primary sponsor: Bayer

Source(s) of monetary or material Support: Bayer A.G.

Intervention

Keyword: Hemophilia A, Lead In

Outcome measures

Primary outcome

Primary Outcome Measures:

Evaluate individual bleeding pattern and bleeding control in hemophilia A patients with clinically severe phenotype treated with FVIII products.

Number of bleeds (all bleeds) per observation time for each participant (annualized bleeding rate (ABR)) [Time Frame: Endpoint will be assessed over the course of the study, from enrollment into the study till the completion. The duration per single patient will be between a minimum of 6 months to a maximum of 12 months.

Secondary outcome

Collect information on patient-reported outcomes (PROs)) and joint status (HJHS score).

Study description

Background summary

Hemophilia A is a bleeding disorder in which the human body does not have enough clotting factor VIII (FVIII), a protein that controls bleeding.
People with severe hemophilia A have no FVIII or < 1% FVIII in their blood This means they may bleed for a long time from minor wounds, have painful bleeding into joints, spontaneous bleeding into joints or muscles or have internal bleeding. In severe hemophilia A the amount of clotting factor VIII in the blood is one percent of the normal amount or less. Bleeding episodes are

more likely.

Study objective

This is a so-called *lead-in study* in which patients receive their standard treatment and no study treatment. The researchers will collect data about the patients* bleeding episodes, FVIII containing treatments used to prevent bleeding episodes and additional FVIII containing treatments used to treat bleeding episodes, as well as how they feel about their symptoms and pain.
After completion of this study, participants can join the gene therapy study with the new treatment BAY2599023. In order to do so they will need to meet the criteria for participation.

Study design

This lead-in study will not have any investigational drug intervention, therefore, no study drug will be administered in the study only standard use of FVIII replacement therapy (NIMP). Previously treated male patients with hemophilia A Approximately 140 patients negative for preexisting immunity against AAVhu37 (Adenoassociated
virus serotype hu37) are planned to be enrolled in this study. Participants will be offered to roll over to the Phase 3 study.

Study burden and risks

No investigational drug is used in this study. This study is a non drug-interventional study
where the treatment is prescribed according to participants* standard of care. There is no
assignment of a patient to a particular therapeutic strategy. The prescription of the medicines
is clearly separated from the decision to include the patient in the study. The risk for the
standard of care treatment is well described. The risks during this study may be related to
blood draws, however, they are considered minor.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Participant must be *18 years of age at the time of signing the informed consent.
- Patients with severe hemophilia A (FVIII:C *1% baseline FVIII activity [FVIII:C] as determined by measurement at the time of screening or from reliable prior documentation in clinical records of the patients).
- Male.
- Previously treated with FVIII concentrate(s) (plasma derived or recombinant) for a minimum of 150 exposure days (ED) as documented in reliable prior clinical records of the patients.
- On regular prophylaxis with FVIII (defined as * 45 weeks/year of treatment with an adequate dose as per label) and on stable treatment for at least 6 months as documented in reliable prior clinical records of the patients
- Well-managed patients with at least 1 documented visit at the hemophilia treatment center in the year prior to enrollment.
- Willing to participate in the interventional Phase 3 gene therapy study with BAY2599023.
- Capable of giving signed informed consent, which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol.

Exclusion criteria

Participants are excluded from the study if any of the following criteria apply. Exclusion criteria marked with an asterisk (*) will lead to exclusion of the participant from the subsequent Phase 3 study, if occurring at any time during the lead-in study. If the criteria marked with an asterisk are met during the study, the participant will withdraw from the study.

Medical Conditions:
- *Current inhibitor to FVIII with a titer * 0.6 BU, confirmed by more than 1 test.
- History of inhibitor with a titer >1.0 BU (as documented in reliable prior clinical records of the patients) or with a repeated titer 0.6 to <1.0 BU in more than one subsequent occasion.
- *Significant underlying liver disease, as evidenced by any of the following: portal hypertension, splenomegaly, ascites, esophageal varices, hepatic encephalopathy,
reduction below normal limits of serum albumin or an advanced liver disease (Child-Pugh Grade B and C), suspicion of liver malignancy or fibrosis by ultrasound / Fibroscan.
- Any of the following:
-- Hemoglobin <;11 g/dL
-- Platelets <100,000 cells/µL
-- Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >1.5× ULN
-- Alkaline phosphatase (AP)>2.5 × ULN
-- Total bilirubin >1.5 × ULN
-- Prothrombin time (PT) or international normalized ratio (INR)>1.0 × ULN
-- Creatinine>1.5 mg/dL
- Another bleeding disorder that is different from hemophilia A (e.g., von Willebrand disease, hemophilia B)
- *Active hepatitis B or C infection, as reflected by HBsAg or HCV-RNA viral load positivity
- Serological evidence of active HIV-1 or HIV-2 as measured by CD4+ cell count <200 cells/mm3 and/or viral load >50 gc/mL.
- *Pre-existing immunity against AAVhu37.
- *Any current diagnosis of malignancy.
- Known or suspected autoimmune diseases requiring immunosuppressive therapy.
- Body mass index >; 35 kg/m^2.
- Contraindication for corticosteroid treatment.
- *Any other significant medical condition that would be a risk to the patient or would affect patient*s ability to receive gene transfer following completion of his participation in this lead-in study.

Prior/Concomitant Therapy
Listed therapies/medications are not allowed at enrollment, during the study and will also not allow transition to the Phase 3 study if introduced during

the lead-in study:
- Antiviral therapy for hepatitis B or C ,
- Pre-medication to tolerate FVIII treatment,
- Immunomodulatory drugs (other than corticosteroids),
- Efavirenz,
- Emicizumab,
- Planned major surgery.

Prior/Concurrent Clinical Study Experience
- Participation in any investigational hemophilia product study within 3 months before screening (participation in any other investigational product study will not be allowed throughout the study).
- Has received the same or another gene therapy product.

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	13
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Factor VIII replacement therapy
Generic name:	N/A
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	01-07-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-11-2021
Application type:	First submission
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	EUCTR2019-004480-48-NL
CCMO	NL77246.042.21
Other	volgt