Screening and Lead-in Observational Protocol to Determine Potential Patient Eligibility for Inclusion in AAV Gene Therapy Clinical Trials in Haemophilia B

Published: 07-04-2021
Last updated: 17-01-2025

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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-OMON54928

Source
ToetsingOnline

Brief title
ECLIPSE

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
bleeding disorder, hemophilia

Research involving
Human

Sponsors and support

Primary sponsor: Freeline Therapeutics

Source(s) of monetary or material Support: Freeline®

Intervention

Keyword: AAV neutralising antibody, Factor IX, Haemophillia B

Outcome measures

Primary outcome

Primary Data:

Bleeding episodes based on a prospective data capture period.

• Date and time of bleed onset and resolution.

• Location of bleed.

• Type of bleed (spontaneous, injury).

• Severity of bleed.

• Concomitant treatments for bleed, if any.

• Response to treatment

Factor IX concentrate consumption based on a prospective data capture period.

• FIX concentrate.

• Dose.

• Dates of administration.

• Reason for administration (prevention, bleeding episode).

• Frequency of administration.

• Total doses.

Secondary outcome

Secondary Data:

Presence/absence of neutralising antibodies to AAVS3.

Baseline clinical parameters related to Haemophilia B:

• Target joint number measured by Target Joint Assessment at enrolment.

• Health Resource Utilisation (usage assessed during Monthly Contact Visits/Calls).

• FIX activity levels (obtained as part of patient standard care, if available).

Study description

Background summary

People with Haemophilia B have very low levels of Factor IX (a protein that is needed for making blood clot properly), and those with the most severe form have frequent bleeding episodes. Where bleeding occurs into joints, this can cause long-term disability and where bleeds occur in a closed space, such as the brain, they can have catastrophic consequences. The current treatment for Haemophilia B is regular (2-3 times per week) intravenous injection (injection into a vein) of Factor IX concentrate to prevent bleeding or on demand treatment when a bleeding episode occurs, for the lifetime of the individual. Both of these modes of treatment have associated limitations and inconveniences.

Study objective

The Sponsor is developing adeno-associated virus (AAV) vector based gene therapies for a number of diseases and is actively advancing a programme in Haemophilia B (HB). This study aims to collect prospective data to characterise bleeding events and Factor IX (FIX) concentrate consumption in HB patients that can be used as baseline for participants who elect to participate in a subsequent gene therapy study of the Sponsor.

Study design

Participants providing consent will attend an enrolment visit either remotely or at the study site to complete eligibility evaluations and receive

instruction for completing the study diary. Demographic data and relevant information to characterise the patient*s HB disease status will be captured. A blood sample will be drawn at a convenient timepoint during the study to assess the participant*s AAV neutralising antibody (NAb) status.

Study burden and risks

This is a prospective data collection study and does not confer any additional risk beyond the normal course of the disease and routine treatment practices. Patient management will be in line with normal standards of care according to the physician treating the patient. No treatment intervention will occur as part of this study.

Contacts

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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)

Elderly (65 years and older)

Inclusion criteria

1) Male participants >= 16 years of age.
2) Able to give full informed consent/assent (according to local regulations) and/or obtain full informed consent from the participant*s legally acceptable representative (as appropriate) and able to understand and comply with all requirements of the study, including diary completion.
3) Interested in participation in future gene therapy clinical studies.
4) Subjects with Haemophilia B with known severe or moderately severe FIX deficiency (<=2% of normal circulating FIX activity) for which the subject is either on
a) Continuous routine FIX prophylaxis*, OR
b) On demand FIX treatment*
5) If receiving prophylaxis, participant has been on stable** and adequate¶ prophylaxis for at least 2 months prior to enrolment

*Continuous routine prophylaxis is defined as the intent of treating with an a priori defined frequency of infusions (e.g., twice weekly, once every two weeks, etc.) as documented in the medical records3.
* Enrollment of on demand patients is competitive up to a maximum of 10 patients.
** Stable denotes subject has been on prophylaxis with no change in either the FIX product used, the dose administered or the regimen in the 2 months prior to enrolment.
¶ Adequate prophylaxis for purposes of this protocol means an annualised bleeding rate (ABR) of <=8 in the year preceding enrolment.

Exclusion criteria

1) Documented evidence of liver fibrosis and/or liver dysfunction (including, but not limited to, persistently elevated alanine aminotransaminase, aspartate aminotransferase, and/or billirubin > 1.5 x upper limit of normal).
2) Prior treatment with a gene transfer medicinal product.
3) Known presence or history of neutralising anti-human FIX antibodies (inhibitors).
4) Previously established serological evidence of HIV-1.
5) Documented active hepatitis B or C, and HBsAg or HCV RNA viral load positivity, respectively, or currently on antiviral therapy for hepatitis B or C. Negative viral assays in 2 samples, collected at least 6 months apart, will be required to be considered negative.
6) Participants at high risk of thromboembolic events (history of arterial or venous thromboembolism [e.g. deep vein thrombosis, pulmonary embolism, non-haemorrhagic stroke, arterial embolus] and those with acquired

thrombophilia. Participants with a history of atrial fibrillation).
7) Known coagulation disorder other than Haemophilia B.
8) Known history of an allergic reaction or anaphylaxis to Factor IX products or known uncontrolled allergic conditions.
9) Known history of allergy to corticosteroids or to tacrolimus or any other macrolide.
10) Known medical condition that would require chronic administration of corticosteroids (excluding topical formulations).
11) History of alcohol or drug dependence.
12) Planned surgical procedure within the next 12 months requiring prophylactic FIX treatment.
13) Known active severe infection (including documented COVID-19 infection), or any other significant concurrent, uncontrolled medical condition evaluated by the investigator to interfere with adherence to the protocol procedures or with tolerance to gene therapy in a future treatment study including, but not limited to, renal, hepatic, cardiovascular, ophthalmological, haematological, immunological, gastrointestinal, endocrine, pulmonary, neurological, cerebral or psychiatric disease, malignancy or any other psychological disorder.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	6
Type:	Anticipated

Ethics review

Approved WMO

Date:	07-04-2021

Application type:	First submission
Review commission:	METC NedMec

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
CCMO	NL74976.041.20
Other	NTC04272554

Study results

Results posted: 13-06-2023

Summary results
Trial never started

First publication
21-03-2023