Prospective study on early immune response to factor VIII exposure in previously untreated patients with severe hemophilia A

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The aim of this study is to characterize the early immune response against F VIII concentrates in patients with severe hemophilia A before and during inhibitor development.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Observational non invasive

Summary

ID

NL-OMON33198

Source
ToetsingOnline

Brief title
PUPS

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
Bleeding disorder, Haemophilia A

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Factor VIII, Hemophilia A, Immune response, Inhibitor

Outcome measures

Primary outcome

- FVIII-specific memory B-cells.

- T-cell characteristics.

- Cytokine/interleukin secretion.

Secondary outcome

- F VIII genotype

- Variation in immune response of certain polymorphisms in IL10, TNFA, CTLA-4

and MHC class II genes

- Copy number variations of FCGR genes

Study description

Background summary

The development of inhibiting antibodies (inhibitors) represents a major challenge in the management of hemophilia A. However, a number of important immunological questions remain unanswered. Insight in the early immune response against exogenous F VIII may ultimately help reduce the risk by preventive measures.

Study objective

The aim of this study is to characterize the early immune response against F VIII concentrates in patients with severe hemophilia A before and during inhibitor development.

Study design

We will perform a prospective study of 20 previously untreated severe hemophilia A patients.

During follow-up of the first 50 exposure days we will obtain clinical relevant data. Blood will be collected prior to each F VIII administration to obtain PBMc for analysis of DNA, T-cell epitopes and F VIII specific B-cell investigation.

Study burden and risks

The only burden of this study may be the drawing of twenty blood samples combined to the first twenty intravenous administrations of F VIII concentrates. Separate venipuncture for the study will be avoided. The total volume of blood collected will not exceed 2*% of the total blood volume expected for a person*s age and weight at any visit.
This burden is in our opinion in proportion to the potential value of the study.
The results of the study may be relevant and beneficial to the patients and their families as well as their treating physicians.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Severe hemophilia A (factor VIII:C <2%)
Previously untreated Patient
Minimally treated patient (< 5 exposures to factor VIII concentrate)

Exclusion criteria

Mild/moderate hemophilia A (factor VIII:C > 2%)
Previously treated patient (>5 exposures to factor VIII concetrate)

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-06-2009
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL28069.018.09