Hemophilia Inhibitor PUP Study

Published: 22-03-2013
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Primary Objectives:- Evaluate changes in the immune system upon exposure to FVIII in patients with severe hemophilia A - Identify immunologic predictors of FVIII inhibitor development or tolerance

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

Summary

ID

NL-OMON39820

Source
ToetsingOnline

Brief title
HIPS

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
Bleeding disorder, Hemophilia A

Research involving
Human

Sponsors and support

Primary sponsor: University of Texas Health Science Center
Source(s) of monetary or material Support: Baxter,Baxter BioScience

Intervention

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

Outcome measures

Primary outcome

Primary Endpoints:

An inhibitor is defined by a Nijmegen test > 0.6 Bethesda units (BU) on two

consecutive tests conducted in the central laboratory.

During the first 50 days of exposure to a single FVIII product:

- Analyze and quantify subclasses of anti-FVIII antibodies

- Characterize FVIII-specific T-cells and changes which occur

- Quantify total FOXP3-positive regulatory T-cells (Treg)

- Assess RNA expression, transcript profile, and exon usage in relevant pathways

- Identify F8 gene mutation and other known genomic predictors of inhibitor

development

- Record infection(s), immunization(s), bleeding episodes, and factor usage

Secondary outcome

N.a.

Study description

Background summary

Hemophilia A is a congenital bleeding disorder caused by deficiency of factor VIII (FVIII) and is treated by replacement therapy with FVIII concentrate. The prevention and treatment of bleeding symptoms is confounded by the development of FVIII neutralizing antibodies, or inhibitors, in approximately 30% of patients with severe hemophilia after exposure to FVIII concentrate. Patients with inhibitors have substantially increased morbidity and increased cost of care. Individual and environmental risk factors for inhibitor formation have been identified, but more information is required before prediction models and prevention strategies can be developed. Furthermore, mechanisms of inhibitor formation and conversely, tolerance to FVIII among patients with hemophilia who

do not develop inhibitors, are poorly understood, limiting the ability to develop rational therapies to overcome inhibitors.

The purpose of the HIPS study is to prospectively evaluate changes in immunity upon exposure to FVIII in patients with severe hemophilia A, and identify immunologic predictors of FVIII inhibitor development or tolerance. The underlying premise of this study is that the type of FVIII-specific T-cell that is activated during the first days of exposure to FVIII determines whether the immune system will develop tolerance to FVIII or develop FVIII inhibitors.

Study objective

Primary Objectives:
- Evaluate changes in the immune system upon exposure to FVIII in patients with severe hemophilia A
- Identify immunologic predictors of FVIII inhibitor development or tolerance

Study design

This is a multinational, multicenter, observational study to evaluate the changes in immunity upon exposure to FVIII in patients with severe hemophilia A previously untreated with factor concentrates. A single source of recombinant FVIII will be used (Advate) and treatment is at the discretion of the investigator. Subjects will be evaluated for 50 days of exposure to FVIII treatment, or three years, whichever comes first. An exposure day is defined as a calendar day during which one or more infusions of FVIII are given.

Study burden and risks

The research question is group related, there is a neglactable risk en minimal burden.
It is important to include children in this study because the research question concerns inhibitor development in hemophilia A, a complication that occurs in the first years of life.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1. An informed consent, approved by the appropriate Institutional Review Board (IRB)/Independent Ethics Committee (IEC), has been administered, signed, and dated.
2. Subject has severe hemophilia A defined by a baseline FVIII:C <0.01 IU/ml. His FVIII activity will be confirmed at the central laboratory. If the confirmatory level is >=0.01 IU/ml the child must exit the study.
3. Subject weighs 3.5 kg or more at the time of his baseline study evaluation

Exclusion criteria

1. Subject has had prior exposure to clotting factor concentrates or blood products, including packed red blood cells (RBC), platelets, plasma, or cryoprecipitate.
2. Subject has a clinically significant chronic disease other than hemophilia A.
3. Subject is currently participating in another investigational drug study.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-05-2013
Enrollment:	2
Type:	Actual

Ethics review

Approved WMO

Date:	22-03-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	01-07-2013
Application type:	Amendment
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	NL42464.018.12