VON WILLEBRAND DISEASE PROPHYLAXIS NETWORK (vWD PN)
The VWD International Prophylaxis (VIP) Study

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The objectives are to:A. Identify subjects with VWD who may benefit from prophylaxis by determining patterns of bleeding prior to evaluation for enrollmentB. Study the effect of prophylaxis on bleeding frequencyC. Establish optimal treatment...

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

Summary

ID

NL-OMON31532

Source
ToetsingOnline

Brief title
VIP-study

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
Von Willebrand disease;

Research involving
Human

Sponsors and support

Primary sponsor: Von Willebrand disease prophylaxis network

Source(s) of monetary or material Support: CSL Behring Marburg, Germany (investigator initiated unrestricted grant),investigator-initiated unrestricted grant van CSL Behring Marburg;Germany

Intervention

Keyword: bleeding, factor VIII, prophylaxis, von Willebrand disease

Outcome measures

Primary outcome

Bleeding episodes. The primary outcome for the study is bleeding episodes associated with VWD. Participants will be provided with diaries on which they will prospectively record the date, location, and cause of hemorrhages occurring during the study. Treatment for breakthrough bleeding episodes and prophylactic doses (date, time, dosage) of VWD product will be recorded as well.

For the menorraghia study the bleeding will be scored using a standardized score (PBAC).

For the arthroscopy study evaluatieon will be performed by a physical therapist using teh WFH PE scale and a pain scale. Radiologic evaluation will be performed using the Petterson score

Health related quaity of life will be assessed by the HRQOL-4.

Secondary outcome

Health economics:

prospective evaluation of absence of scholl or work

product usage

hospitalizations

laboratory analysis : inhibitors to VWF

Safety variables:

serious adverse events

other adverse events

Study description

Background summary

Von Willebrand factor (VWF) is a multimeric plasma glycoprotein that is synthesized in megakaryocytes and endothelial cells. It circulates in plasma in the form of multimers with a size ranging from 500 to approximately 20,000 kDa. VWF mediates and contributes to platelet aggregation and the adhesion of the initial platelet plug to the subendothelium of the injured blood vessels. It also serves as the plasma carrier protein for factor VIII (FVIII) [Handin & Wagner, 1989], with which it forms a non-covalently bound complex (FVIII/VWF complex) [Hoyer, 1981].

Abnormalities of VWF (deficiency or dysfunction) result in von Willebrand disease (VWD), a common hereditary bleeding disorder that may affect as much as 1% of the general population [Rodeghiero et al., 1987]. The inheritance modus is mostly autosomal dominant, but sometimes is autosomal recessive or double heterozygous; the disorder affects both sexes. The impaired formation and adhesion of the initial platelet plug is reflected in the prolonged platelet function assay (PFA) test or skin bleeding time (BT). In addition, reduced levels of von Willebrand factor ristocetin cofactor (VWF:RCo) activity, von Willebrand factor antigen (VWF:Ag), factor VIII coagulation activity (FVIII:C), factor VIII antigen (FVIII:Ag), and abnormalities of the multimeric structure of VWF are variably found among the several types and subtypes of VWD.

Clinically, the leading symptom in VWD is bleeding, chiefly of mucosal type, e.g. epistaxis, gingival or GI bleeding, and menorrhagia. In severe forms of VWD with secondary deficiency of FVIII, spontaneous joint and muscular bleeding, resembling those observed in severe hemophilia A, may also be observed.

Study objective

The objectives are to:
A. Identify subjects with VWD who may benefit from prophylaxis by determining patterns of bleeding prior to evaluation for enrollment
B. Study the effect of prophylaxis on bleeding frequency
C. Establish optimal treatment regimens for joint bleeding, GI bleeding, epistaxis, and menorrhagia
D. Determine how quality of life at baseline is related to bleeding history prior to enrollment and whether changes in bleeding frequency during follow-up are associated with changes in quality of life at the conclusion of follow-up
E. Identify the frequency of development of inhibitory antibodies to VWF
F. Study the frequency and indications for hospitalizations
G. Evaluate the safety of prophylaxis by tracking study-related adverse events

Other goals include a retrospective study of the effect of prophylaxis on bleeding frequency, and a retrospective natural history study of GI bleeding in VWD.

Study design

The VIP study is observational in design. Participants will not be randomized. VWF/FVIII products labeled for VWD will be chosen for use at the discretion of the participating investigator. Products used to treat study participants will not be provided as part of the study. Treatment of acute bleeding episodes and management of treatment failure, such as severe breakthrough bleeding not adequately controlled by the dose escalation schedule will be at the discretion of the investigator. Participants enrolled in the prospective phase will undergo an escalation of treatment from one to three dose levels of VWD product. It is assumed that all subjects enrolled will begin treatment on the level one dose and remain on this dose for the duration of follow-up, or until they meet the criteria for escalation to level two or three (if indeed they do meet the criteria).

Intervention

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escalation to level two or three (if indeed they do meet the criteria).

Study burden and risks

The additional burden for the patients is limited because profylactic use of coagulation factor concentrates in patients with VWD is already widely used in the Netherlands. The criteria for start of prophylaxis are however not clearly defined. This is also the case for dosage and frequncy of coagulation factor ceonccentrate infusions. This is the main research question of this study. The risk are small and are mainly the occurrence of inhibitory antibodies (only in type 3 patients) against VWF (< 5%), athough the real incidence in type 3 VWD is unknown.

Contacts

Public
Von Willebrand disease prophylaxis network

p.a. Rho Inc. 6330 Quadrangle drive
NC 27517 Chapel Hill
US
Scientific
Von Willebrand disease prophylaxis network

p.a. Rho Inc. 6330 Quadrangle drive
NC 27517 Chapel Hill
US

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

A. Type 1: eligible for participation if
1. < or = 20% RCo and/or < or = 20% FVIII; and
2. DDAVP non-responsive, defined as occurrence of bleeding episodes not responding satisfactorily to desmopressin, or deemed non-responsive a priori by the investigator; and
3. Bleeding indication criteria are met (page 9-11 protocol) . ;B. Type 2: eligible for participation if
1. DDAVP non-responsive, defined as occurrence of bleeding episodes not responding satisfactorily to desmopressin, or deemed non-responsive a priori by the investigator; or Type 2B; and
2. Bleeding indication criteria are met (page 9-11 protocol) ;C. Type 3: eligible for participation if
1. Bleeding indication criteria are met (page 9-11 protocol)

Exclusion criteria

A. They have acquired VWD;B. They have a history of inhibitory antibodies to VWF;C. They are already on prophylaxis, defined as receiving factor infusions at least once per week to prevent or decrease the severity of bleeding with the intention of maintaining this regimen for, on average, 45 or more weeks per year; or are receiving factor infusions on a regular basis to prevent or decrease the severity of menorrhagia.

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	01-10-2009
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Humate P
Generic name:	Factor VIII/ von Willebrand factor concentrate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Immunate SD
Generic name:	Factor VIII/ von Willebrand factor concentrate
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	18-08-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-07-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-11-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2007-004943-31-NL
CCMO	NL18951.078.08