Type 3 Von Willebrand International Registries Inhibitor Prospective Study Extended.

Published: 12-02-2014
Last updated: 01-05-2024

- International network among European (125 cases) and Iranian (125 cases) centers- Prospective enrollment of the 250 VWD3 patients using a common database online- Detailed information about previous bleedings and exposure to VWF concentrates-...

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

Summary

ID

NL-OMON50286

Source
ToetsingOnline

Brief title
3WINTERS-IPS EXTENDED

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Blood and lymphatic system disorders congenital

Synonym
Von Willebrand disease;

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Fondazione Angelo Bianchi Bonomi;a non-

profit organization located in Milan;Italy

Intervention

Keyword: Factor VIII, Prospective study, Type 3 Von Willebrand's Disease, Von Willebrand antigen, von Willebrand factor

Outcome measures

Primary outcome

First part of the study:

- Informed consent

- Eligibility verification

- Patient ID assignment

- Demographics

- Bleeding history and previous use of blood components

- General laboratory test with local assays for VWD3 diagnosis

- Family history in the parents and relatives

- Blood withdrawal for central laboratory assessment

- Mutation analysis in VWD3

- Inhibitor assessment

Optional in the relatives:

- Informed consent

- Historical information

- Blood sampling for local laboratory assessment

Secondary outcome

Second part of the study (4 years):

- Bleeding episodes

- VWF concentrates

- Blood withdrawal for central laboratory assessment only in case of anti-VWF

inhibitors

Study description

Background summary

Von Willebrand Disease (VWD) is the most common inherited bleeding disorder, characterized by a quantitative (VWD types 1 and 3) and/or qualitative (VWD types 2A, 2B, 2M and 2N) deficiency of von Willebrand factor (VWF), the large multifunctional plasma glycoprotein that plays a major role in early phases of haemostasis. VWD type 3 (VWD3) is due to virtually complete deficiency of VWF and, for this reason, has also been described as 'severe VWD'. In fact, VWD3 patients by definition are characterized by undetectable levels of VWF antigen (VWF:Ag) in plasma and reduced concentrations (<10 IU/dL) of factor VIII (FVIII). These baseline levels usually do not increase in plasma following desmopressin (DDAVP), the drug which can release VWF from endothelium. VWD3 is inherited as a recessive trait and heterozygous relatives have mild or no bleeding symptoms. The prevalence of VWD3 is very low, ranging from 0.1-5.3 per million and differing considerably between countries. The highest rate is found in Iran and the lowest in southern Europe. However, the actual prevalence of VWD3 is still unknown in most countries, due to the lack of retrospective or prospective studies. Although rare, VWD3 is of major interest because its severe clinical presentation, the need for replacement therapy with VWF concentrates (until now only plasma-derived VWF concentrates are available but a recombinant VWF is under clinical trial) and the risk of occurence of anti-VWF inhibitors after the infusion of VWF concentrates, for which risk factors have not been systematically determined.

Study objective

- International network among European (125 cases) and Iranian (125 cases) centers
- Prospective enrollment of the 250 VWD3 patients using a common database online
- Detailed information about previous bleedings and exposure to VWF concentrates

- Bleeding severity score of VWD3 calculated with a common questionnaire
- Plasma and DNA samples from all 250 patients for centralized analyses
- Confirmation of the diagnoses using centralized tests
- VWF gene defects with VWF phenotype and risk of anti-VWF inhibitors
- Common methods for anti-VWF antibody determination and for gene analyses in VWD3
- Frequency and sites of bleeding in VWD3 followed-up for 2 years
- Efficacy assessment of the VWF concentrates used to treat VWD3 using the mos objective criteria for efficacy

Study design

A no-profit, investigators initiated, multicenter, European-Iranian, observational, retrospective and prospective study on patients with diagnosis VWD3.

Study burden and risks

If the patient agrees to participate in the trial, an appointment will be made at the treatment center for the first part of the trial. A medical doctor involved in this research will explain the study to the patient, ask some questions concerning the medical history, bleeding history, all the treatments received and will ask to provide previous laboratory assessments and results and finally have a sample of blood taken. All these procedures will be done in a single visit.
In the second part of the study, if the patient is centrally confirmed to be VWD3 subject, he or she will be asked to attend the medical center according to the visits scheme foreseen by the center standards for a total of 4 years. There are not pre-scheduled visit required by this study and visits at the center will be agreed between the patient and the doctor according to the standard care of the center, at least once per year. At each visit (independently on when it occurs), the patient will be asked to provide information on concomitant medications and treatments used, bleedings and other adverse experiences occurred since the last visit.
The patient will not be asked to take any medication. The blood sampling will take short time and involve a small amount of pain.
Hopefully the study will lead to a more accurate way of diagnosis and management of VWD3. This will help the patient directly in being confirmed whether he or she has VWD with a higher degree of certainty and will also allow for a more accurate and easier way of diagnosing the disease in other patients.

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)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

- Male and female of any age, including infants, children, adolescents and adults
- Informed consent obtained (parents should sign for patients < 18 y.o.)
- Previous diagnosis of VWD3 (VWF antigen: undetectable or < 5 U/dL)
- Detailed information on inherited pattern, history of bleeding, previous exposure to blood products
- Availability of plasma and DNA samples

Exclusion criteria

- VWD3 patients who may not be available for follow-up

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-07-2014
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	12-02-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-07-2020
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
CCMO	NL40272.078.12