A Phase II/III, multicenter, partially randomized, open label trial investigating safety and efficacy of on-demand and prophylactic treatment with BAY 94-9027 in Severe Hemophilia A

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PART A: To assess the efficacy of BAY 94-9027 in prevention and treatment of bleeding at different infusion schedules.PART B: To assess the safety and efficacy of BAY 94-9027 in the prevention of bleeding during major surgical procedures.

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

Summary

ID

NL-OMON45106

Source
ToetsingOnline

Brief title
PROTECT VIII

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
Hemophilia A

Research involving
Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: Bayer B.V.

Intervention

Keyword: Factor VIII, Hemophilia A, Profylaxis

Outcome measures

Primary outcome

Total number of bleedings as reported by the subjects (efficacy)

Secondary outcome

- questionnaires (evaluate subject*s assessment)

- adverse events (safety and tolerability)

- pharmacokinetics and incremental recovery following administration of Bay

94-9027

- questionnaires for quality of life, work productivity and pain

Study description

Background summary

BAY 94-9027 could provide a clinical benefit in subjects with severe hemophilia A in preventing bleeds. This could decrease the number of infusions with FVIII.

See protocol page 16-19

Study objective

PART A: To assess the efficacy of BAY 94-9027 in prevention and treatment of bleeding at different infusion schedules.
PART B: To assess the safety and efficacy of BAY 94-9027 in the prevention of bleeding during major surgical procedures.

Study design

Design PART A: The study consists of an up to 36-week treatment period.
On-demand treatment arm: subjects will receive BAY 94-9027 for on demand treatment of acute bleeding events for 36 weeks.
Prophylactic treatment arm: subjects receive regularly scheduled infusion as per treatment arm assignment. All subjects entering the prophylaxis arm will start with 2x/week infusion. Following a clinical assessment at Week 10, a subset of subjects will continue in the 2x/week treatment arm for an additional 26 weeks. All others will be randomized 1:1 to either an every 5 days or every 7 days prophylactic infusion for an additional 26 weeks.
For all subjects, infusions and bleeding events will be documented in an electronic subject diary (ePD) throughout the study.
The subjects* health, quality of life, measurements of in vivo recovery, and any inhibitor or antibody development will be assessed at specific intervals.

Design PART B:
Part B is open to all subjects participating in Part A and to individuals with severe hemophilia A, requiring a major surgery, not otherwise enrolled in this clinical study who meet the same inclusion and exclusion criteria as required in Part A. Subjects may participate in Part B more than once.

Intervention

There will be 4 treatment arms:
- An on-demand group
- Twice a week
- Once every 5 days
- Once a week

The trial can be divided in the following phases:
- Screening phase (for all patients)
- patients in the on-demand group
- All subjects entering the prophylaxis arm will start with 2x/week infusion. Subjects in prophylactic treatment arms will undergo clinical evaluation at 10 weeks. Those with adequate control of bleeding will undergo randomization to every 5 or 7 day infusion. Those with continued bleeding will remain in treatment arm and have an increase in dose.

The total duration of the treatment is 36 weeks.

Extension study:
The purpose of the extension phase is to provide further observations on the safety and efficacy of BAY 94-0927. It is asked that all subjects participating remain in the extension until they have accumulated at least 100 total days of treatment (including the treatments received in the main study). If you decide

to participate in the study, you will be asked to continue treatment until you have received 100 total days of treatment with BAY 94-9027. This may take between at least 6 to12 months depending upon your frequency of infusion or how often you have bleeds. If you have already or will soon have 100 days, you may be in the extension for at least 6 months, and for as long as it is running.

Study burden and risks

- 10 hospital visits
- Physical examination (3x)
- Hart rate, blood pressure (6x)
- Joint assessment (Gilbert-score) (1x)
- Weight(5x)
- ECG (1x)
- Lab (7x)
- Questionnaires at three visits
- Possible adverse events

Contacts

Public
Bayer

Energieweg 1
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Scientific
Bayer

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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Male; 12 to 65 years of age (or Male 18-65 years of age in countries where enrollment of minors is not permitted)
* Subjects with severe hemophilia A (baseline FVIII activity FVIII:C <1%) determined by measurement at the time of screening or from reliable prior documentation (eg, measurement in other clinical trials, result from approved clinical laboratory)
* Previously treated with FVIII concentrate(s) (plasma derived or recombinant) for a minimum of 150 ED
* Immunocompetent. If HIV positive, CD4+ lymphocyte count >200/mm3

Exclusion criteria

* Current evidence of inhibitor to FVIII with a titer * 0.6 BU/mL, measured by the Nijmegen modified Bethesda assay at the time of screening (central laboratory) (BU: Bethesda unit)
* History of inhibitor to FVIII with a titer * 0.6 BU, or clinical history suggestive of inhibitor requiring modification of treatment. Subjects with a maximum historical titer of 1.0 BU on a single measurement but with at least 3 subsequent successive negative results (< 0.6 BU) thereafter are eligible
* Any other inherited or acquired bleeding disorder in addition to Hemophilia A
* Platelet count < 100,000/mm3
* Creatinine > 2x upper limit of normal
* AST or ALT > 5x upper limit of normal (AST: aspartate aminotransferase; ALT: alanine aminotransferase)
* The subject is currently participating in another investigational drug study, or has participated in a clinical study involving an investigational drug within 30 days of study entry. Subjects who are currently participating in an investigational study in which they are treated with a currently marketed FVIII concentrate are not excluded. Subjects currently treated with BAY 81-8973, and who have received at least 100 ED with the investigational product, may continue treatment with the product up to the start of Visit 1.
* Any subject who is receiving chemotherapy, immune modulatory drugs other than anti-retroviral chemotherapy, or chronic use of oral or intravenous (IV) corticosteroids within the last 3 months. Brief courses of prednisone/methyprednisolone (< 14 days) for treatment of disorders such as synovitis, asthma, etc are allowed at the discretion of the treating physician.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-10-2012
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BAY 94-9027 (niet beschikbaar)
Generic name:	NVT

Ethics review

Approved WMO Date:	21-05-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-07-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-09-2012
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-11-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-11-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-01-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-03-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-04-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-08-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-09-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-10-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-11-2013
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-11-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-11-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-12-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-12-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-05-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-08-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-09-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-09-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-11-2014
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-12-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-12-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-01-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-02-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-10-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-10-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-10-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-01-2017
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-02-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-04-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-04-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-08-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-10-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-10-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-11-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-05-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-07-2018
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-10-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-12-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-01-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-02-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2011-005210-11-NL
ClinicalTrials.gov	NCT01580293
CCMO	NL40664.042.12